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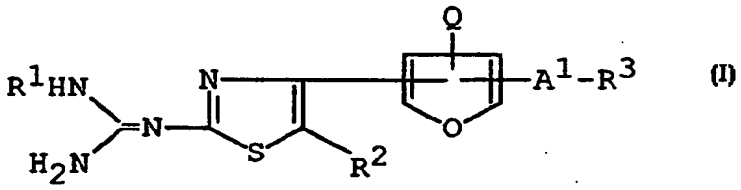

(I)

(57) Abstract

This invention relates to furylthiazole derivatives represented by formula (I), wherein each symbol is as defined in the specification and pharmaceutically acceptable salts thereof which have antiulcer activity, H_2-receptor antagonism and antimicrobial activity, to processes for the preparation thereof, to a pharmaceutical composition comprising the same and to a method for the treatment of ulcer and infectious diseases in human being or animals.

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DESCRIPTION

Furylthiazole and their use as H_2-receptor antagonism and antimicrobial.

Technical Field

This invention relates to new furylthiazole derivatives and pharmaceutically acceptable salts thereof useful as a medicament.

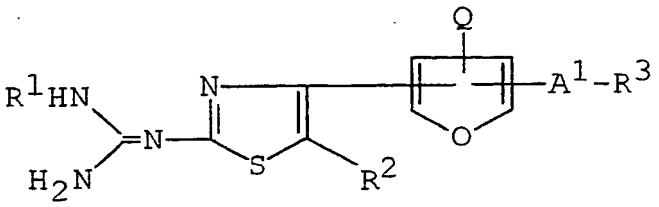
Background Art

In European Patent Application Publication No. 355,612, furylthiazole derivatives having antiulcer activity and H_2-receptor antagonism are disclosed.

Disclosure of the Invention

This invention relates to furylthiazole derivatives and pharmaceutically acceptable salts thereof which have antiulcer activity, H_2-receptor antagonism and antimicrobial activity, to processes for the preparation thereof, to a pharmaceutical composition comprising the same and to a method for the prevention and/or the treatment of ulcer and/or infectious diseases in human being or animals.

The furylthiazole derivatives of this invention are new and can be represented by the following general formula (I) :



(I)

wherein

R^1 is n-pentyl, branched(lower)alkyl,
branched(lower)alkenyl, lower alkenyl having
(lower)alkoxy, higher alkyl,
cyclo(lower)alkyl(lower)alkyl,
cyclo(lower)alkylidene(lower)alkyl,
cyclo(lower)alkenyl(lower)alkyl,
lower alkylthio(lower)alkyl,
aryl which may have one or more suitable
substituent(s),
ar(lower)alkyl which may have one or more
suitable substituent(s),
aryloxy(lower)alkyl which may have one
or more suitable substituent(s),
ar(lower)alkoxy(lower)alkyl which may have one
or more suitable substituent(s),
higher alkenyl which may have one or more
suitable substituent(s),
propoxypropyl, ethoxypropyl, butoxypropyl,
propoxyethyl, butoxyethyl, butoxybutyl,
methoxybutyl, ethoxybutyl,
lower alkoxy(lower)alkoxy(lower)alkyl,
arylamino(lower)alkyl which may have one or
more suitable substituent(s),
pyridin-4-yl(lower)alkyl,
pyridin-3-yl(lower)alkyl,
lower alkyl-substituted pyridyl(lower)alkyl,
imidazolyl(lower)alkyl or

a group of the formula :

$$-A^2-R^4$$

[wherein

A^2 is lower alkylene or lower alkenylene, and

R^4 is unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s),

unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) which may have one or more suitable substituent(s),

unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atom(s),

saturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s),

saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) or

unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) which may have one or more suitable substituent(s),]

R^2 is hydrogen or lower alkyl,

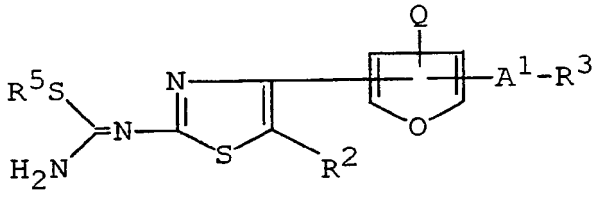
R^3 is amino or acylamino,

A^1 is lower alkyl,

Q is hydrogen or lower alkyl.

The object compound (I) or a salt thereof can be prepared by processes as illustrated in the following reaction schemes.

Process 1



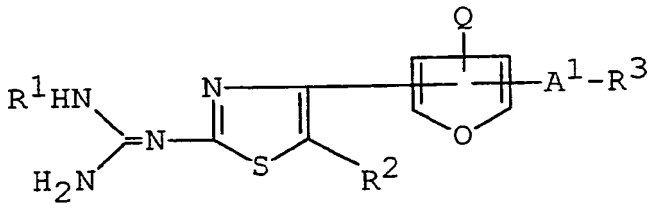
(II)

or a salt thereof

R^1-NH_2

(III)

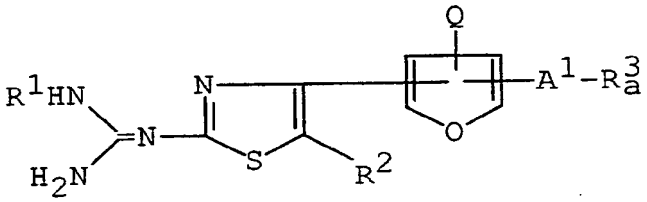
or a salt thereof



(I)

or a salt thereof

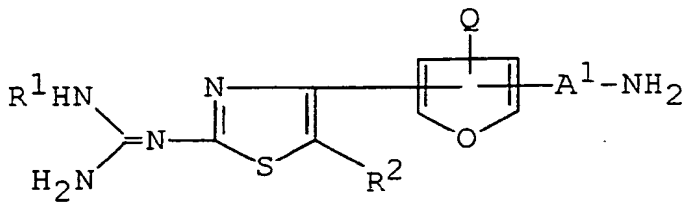
Process 2



(Ia)

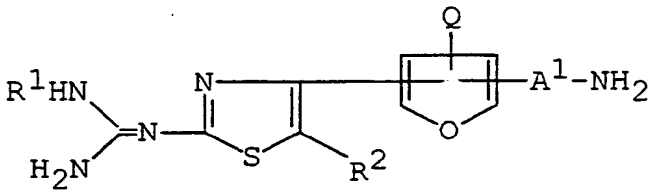
or a salt thereof

Deacylation



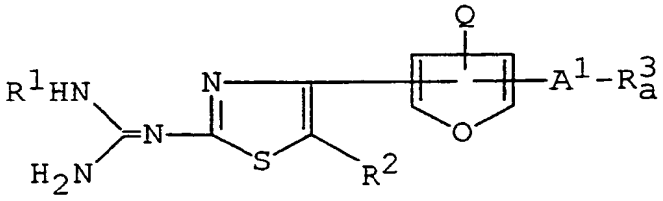
(Ib)
or a salt thereof

Process 3



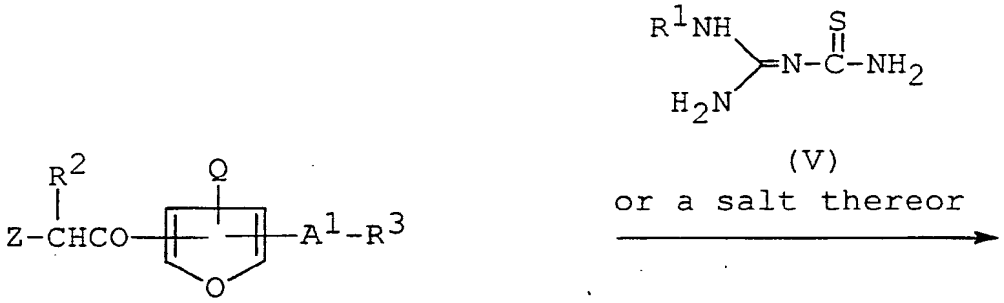
acylation

(Ib)
or a salt thereof



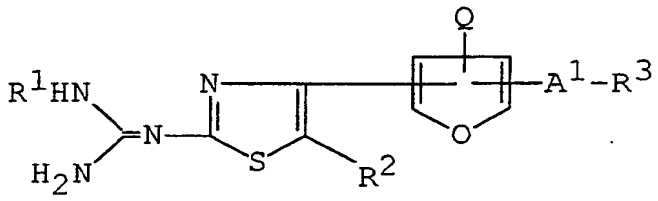
(Ia)
or a salt thereof

Process 4



(IV)
or a salt thereof

(V)
or a salt thereor

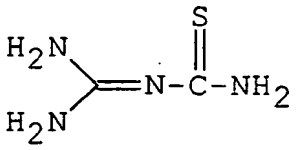


(I)
or a salt thereof

wherein R^1, R^2, R^3, A^1 and Q are each as defined above,
R^3_a is acylamino,
R^5 is lower alkyl, and
Z is acid residue.

The starting compound (V) or a salt thereof can be prepared by the following processes.

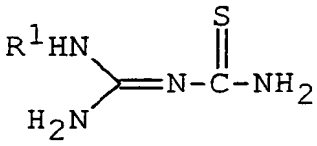
Process A



(VI)
or a salt thereof

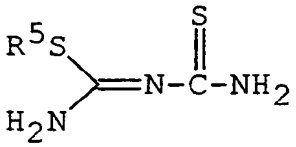
R^1-NH_2

(III)
or a salt thereof



(V)
or a salt thereof

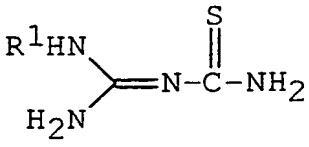
Process B



(VII)
or a salt thereof

R^1-NH_2

(III)
or a salt thereof



(V)
or a salt thereof

wherein R^1 and R^5 are each as defined above.

In the above and subsequent description of the present specification, suitable examples of the various definitions to be included within the scope of the invention are explained in detail in the following.

The term "lower" is intended to mean a group having 1 to 6 carbon atom(s), preferably 1 to 4 carbon atom(s), unless otherwise provided.

The term "higher" is intended to mean a group having 7 to 20 carbon atoms, unless otherwise provided.

Suitable "one or more" in the term "one or more suitable substituent(s)" is intended to mean the number of 1 to 4.

Suitable "branched(lower)alkyl" may include isopropyl, 1-methylpropyl, 1-ethylpropyl, isobutyl, sec-butyl, tert-butyl, 2-ethylbutyl, 3-ethylbutyl, isopentyl, neopentyl, tert-pentyl, 1-methylbutyl, 2-methylbutyl, 3,3-dimethylbutyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, isohexyl, and the like, in which the preferred one may be branched(C_3-C_6)alkyl, and the most preferred one may be isopropyl, isobutyl, neopentyl, 2-methylbutyl, isopentyl, 4-methylpentyl, 1-ethylpropyl, 2-ethylbutyl and 2-methylpentyl.

Suitable "branched lower alkenyl" may include 1-(or 2-)methylvinyl, 1-(or 2- or 3-)methyl-1-butenyl, 1-(or 2- or 3-)methyl-2-butenyl, 1-(or 2- or 3- or 4-)methyl-1-pentenyl, 1-(or 2- or 3- or 4-)methyl-2-pentenyl, 1-(or 2- or 3- or 4-)methyl-3-pentenyl, 1-(or 2- or 3- or 4-)methyl-4-pentenyl, and the like, in which the preferred one may be branched(C_2-C_6)alkenyl, and the most preferred one may be 3-methyl-2-butenyl and 4-methyl-3-pentenyl.

Suitable "lower alkenyl having (lower)alkoxy" may include 1-(or 2-)methoxy-3-butenyl, 1-(or 2-)ethoxy-3-butenyl, 4-methoxy-(1- or 2- or 3-)butenyl, 4-ethoxy-(1- or 2- or 3-)butenyl, and the like, in which the preferred

one may be (C_2-C_6)alkenyl having (C_1-C_6)alkoxy, and the most preferred one may be 2-ethoxy-3-butenyl and 4-ethoxy-2-butenyl.

Suitable "higher alkyl" may be a straight or branched one such as heptyl, octal, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl, icosanyl, or the like, in which the preferred one may be (C_7-C_{10})alkyl, the more preferred one may be (C_7-C_8)alkyl and the most preferred one may be n-heptyl and n-octyl.

Suitable "lower alkyl" may be a straight or branched one such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl, or the like, in which the preferred one may be (C_1-C_4)alkyl and the most preferred one may be methyl, ethyl and n-propyl.

Suitable "cyclo(lower)alkyl" moiety in the term of "cyclo(lower)alkyl(lower)alkyl" may include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

Suitable "lower alkyl" moiety in the term of "cyclo(lower)alkyl(lower)alkyl", "cyclo(lower)alkylidene(lower)alkyl" and "cyclo(lower)alkenyl(lower)alkyl" can be referred to aforementioned "lower alkyl".

Suitable "cyclo(lower)alkylidene" moiety in the term of "cyclo(lower)alkylidene(lower)alkyl" may include cyclopropylidene, cyclobutylidene, cyclopentylidene, cyclohexylidene, and the like, in which the preferred one may be cyclo(C_3-C_6)alkylidene, and the most preferred one may be cyclohexylidene.

Suitable "cyclo(lower)alkenyl" moiety in the term of "cyclo(lower)alkenyl(lower)alkyl" may include cyclopropenyl, cyclobutenyl, 1,3-cyclobutadienyl, cyclopentenyl, 2,4-cyclopentadienyl, cyclohexenyl, 2,5-cyclohexadienyl, and the like, in which the preferred one may be cyclo(C_3-C_6)alkenyl, and the most preferred one

may be cyclohexenyl.

Suitable "lower alkylthio(lower)alkyl" may include methylthiomethyl, methylthioethyl, 1-(or 2-)-methylthioethyl, 1-(or 2- or 3-)methylthiopropyl, ethylthiomethyl, ethylthioethyl, 1-(or 2-)ethylthioethyl, 1-(or 2- or 3-)ethylthiopropyl, propylthiomethyl, propylthiopropyl, 1-(or 2-)propylthioethyl, 1-(or 2- or 3-)propylthiopropyl, isopropylthiomethyl, 1-(or 2-)-isopropylthioethyl, 1-(or 2- or 3-)isopropylthiopropyl, and the like, in which the preferred one may be (C_1-C_6)-alkylthio(C_1-C_6)alkyl, and the most preferred one may be methylthioethyl.

Suitable "aryl" moiety in the term of "aryl which may have one or more suitable substituent(s)" may include phenyl, naphthyl, anthryl, and the like, in which the preferred one may be (C_6-C_{10})aryl, and the most preferred one may be phenyl and naphthyl.

Suitable "lower alkyl" moiety in the term "ar(lower)alkyl" can be referred to aforementioned "lower alkyl".

Suitable examples of "suitable substituent(s)" moiety in the terms of "aryl which may have one or more suitable substituent(s)", "ar(lower)alkyl which may have one or more suitable substituent(s)", "aryloxy(lower)alkyl which may have one or more suitable substituent(s)", "ar(lower)alkoxy(lower)alkyl which may have one or more suitable substituent(s)", "arylamino(lower)alkyl which may have one or more suitable substituent(s)", "unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) which may have one or more suitable substituent(s)" and "unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) which may have one or more suitable substituent(s)" may include lower alkyl (e.g., methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-

butyl, pentyl, neopentyl, t-pentyl, hexyl, etc.), lower alkoxy (e.g., methoxy, ethoxy, propoxy, isopropoxy, isobutoxy, t-butoxy, pentyloxy, neopentyloxy, t-pentyloxy, hexyloxy, etc.), lower alkenyl (e.g., vinyl, 1-propenyl, allyl, 1-methylallyl, 1-(or 2 or 3-)butenyl, 1-(or 2- or 3- or 4-)pentenyl, 1-(or 2- or 3- or 4- or 5-)hexenyl, etc.), lower alkynyl (e.g., ethynyl, 1-propynyl, propargyl, 1-methylpropargyl, 1-(or 2- or 3-)butynyl, 1-(or 2- or 3- or 4-)pentynyl, 1-(or 2- or 3- or 4- or 5-)hexynyl, etc.), mono-(or di- or tri-)-halo(lower)alkyl (e.g., fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, bromomethyl, dibromomethyl, tribromomethyl, 1-(or 2-)fluoroethyl, 1-(or 2-)bromoethyl, 1-(or 2-)chloroethyl, 1,1-difluoroethyl, 2,2-difluoroethyl, etc.), halogen (e.g., chloro, bromo, fluoro, iodo), carboxy, protected carboxy as mentioned below, hydroxy, protected hydroxy as mentioned below, aryl (e.g., phenyl, naphthyl, etc.), ar(lower)alkyl such as phenyl(lower)alkyl (e.g. benzyl, phenethyl, phenylpropyl, etc.), carboxy(lower)alkyl, protected carboxy(lower)alkyl, nitro, amino, protected amino as mentioned below, di-(lower)alkylamino (e.g., dimethylamino, diethylamino, diisopropylamino, ethylmethylamino, isopropylmethylamino, ethylmethylamino, ethylpropylamino, etc.), hydroxy(lower)alkyl, protected hydroxy(lower)alkyl, acyl as mentioned below, cyano, mercapto, lower alkylthio (e.g., methylthio, ethylthio, propylthio, isopropylthio, butylthio, etc.), imino, carbamoyl, sulfamoyl, aryloxy(lower)alkyl (e.g., phenoxymethyl, phenoxyethyl, phenoxypropyl, naphthyloxymethyl, naphthyloxyethyl, naphthyloxypropyl, etc.), heterocyclic group as mentioned below, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl (e.g., methylaminosulfonyl, dimethylaminosulfonyl, ethylaminosulfonyl,

diethylaminosulfonyl, etc.), lower alkoxy(lower)alkoxy (e.g., methoxymethoxy, methoxyethoxy, ethoxymethoxy, ethoxyethoxy, etc.), protected carboxy(lower)alkoxy, mono- or di-(lower)alkylcarbamoyl(lower)alkoxy (e.g. methylcarbamoylmethoxy, dimethylcarbamoylmethoxy, ethylcarbamoylethoxy, diethylcarbamoylethoxy, etc.), and the like,

in which the preferred one may be (C_1-C_6)alkyl, (C_1-C_6) alkoxy, halogen, nitro, sulfamoyl, aryloxy(C_1-C_6)alkyl, heterocyclic group, heterocyclic(C_1-C_6)alkyl, mono- or di-(C_1-C_6)alkylaminosulfonyl, mono-(or di- or tri-)-halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, protected-carboxy(C_1-C_6)alkoxy, mono- or di-(C_1-C_6)alkylcarbamoyl-(C_1-C_6)alkoxy,

and the most preferred one may be methyl, methoxy, ethoxy, propoxy, isopropoxy, chloro, fluoro, trifluoromethyl, nitro, amino, acetylamino, hydroxy, piperidyl, piperidylmethyl, phenoxymethyl, N,N-dimethylsulfonyl, methoxyethoxy, ethoxycarbonylethyl and N,N-dimethylcarbamoylmethoxy.

Suitable "protected carboxy" moiety in the term of "protected carboxy", "protected carboxy(lower)alkyl" and "protected carboxy(lower)alkoxy" may include esterified carboxy.

And suitable example of said ester may be the ones such as lower alkyl ester (e.g., methyl ester, ethyl ester, propyl ester, isopropyl ester, butyl ester, isobutyl ester, t-butyl ester, pentyl ester, t-pentyl ester, hexyl ester, etc.);

lower alkenyl ester (e.g., vinyl ester, allyl ester, etc.); lower alkynyl ester (e.g., ethynyl ester, propynyl ester, etc.); lower alkoxy(lower)alkyl ester (e.g., methoxymethyl ester, ethoxymethyl ester, isopropoxy ester, 1-methoxyethyl ester, 1-ethoxyethyl ester, etc.); lower alkylthio(lower)alkyl ester (e.g., methylthiomethyl ester,

ethylthiomethyl ester, ethylthioethyl ester, isopropoxythiomethyl ester, etc.); mono-(or di- or tri-)-halo(lower)alkyl ester (e.g., 2-iodoethyl ester, 2,2,2-trichloroethyl ester, etc.); lower alkanoyloxy(lower)alkyl ester (e.g., acetoxymethyl ester, propionyloxyethyl ester, butyryloxymethyl ester, valeryloxymethyl ester, pivaloyloxymethyl ester, hexanoyloxymethyl ester, 1-acetoxyethyl ester, 2-acetoxyethyl ester, 2-propionyloxyethyl ester, etc.); lower alkoxycarbonyloxy(lower)alkyl ester (e.g., methoxycarbonyloxymethyl ester, ethoxycarbonyloxymethyl ester, propoxycarbonyloxymethyl ester, 1-(or 2-)[methoxycarbonyloxy]ethyl ester, 1-(or 2-)[ethoxycarbonyloxy]ethyl ester, 1-(or 2-)[propoxycarbonyloxy]ethyl ester, 1-(or 2-)[isopropoxycarbonyloxy]ethyl ester, etc.); lower alkanesulfonyl(lower)alkyl ester (e.g., mesylmethyl ester, 2-mesylethyl ester, etc.); lower alkoxycarbonyloxy(lower)alkyl ester (e.g., methoxycarbonyloxymethyl ester, ethoxycarbonyloxymethyl ester, propoxycarbonyloxymethyl ester, t-butoxycarbonyloxymethyl ester, 1-(or 2-)methoxycarbonyloxyethyl ester, 1-(or 2-)ethoxycarbonyloxyethyl ester, 1-(or 2-)isopropoxycarbonyloxyethyl ester, etc.); phthalidylidene(lower)alkyl ester, or (5-lower alkyl-2-oxo-1,3-dioxol-4-yl)(lower)alkyl ester [e.g., (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl ester, (5-ethyl-2-oxo-1,3-dioxo-4-yl)methyl ester, (5-propyl-2-oxo-1,3-dioxol-4-yl)ethyl ester, etc.]; ar(lower)alkyl ester, for example, phenyl(lower)alkyl ester which may have one or more suitable substituent(s) (e.g., benzyl ester, 4-methoxybenzyl ester, 4-nitrobenzyl ester, phenethyl ester, trityl ester, benzhydriyl ester, bis(methoxyphenyl)methyl ester, 3,4-dimethoxybenzyl ester,

4-hydroxy-3,5-di-t-butylbenzyl ester, etc.); aryl ester which may have one or more suitable substituent(s) such as substituted or unsubstituted phenyl ester (e.g., phenyl ester, tolyl ester, t-butylphenyl ester, xylyl ester, mesityl ester, cumenyl ester, 4-chlorophenyl ester, 4-methoxyphenyl ester, etc.); tri-(lower)alkyl silyl ester; lower alkylthioester (e.g., methylthioester, ethylthioester, etc.) and the like.

Suitable "protected amino" may include an "acylamino" as mentioned below or an amino group substituted by a conventional protecting group such as ar(lower)alkyl which may have suitable substituent(s) (e.g., benzyl, trityl, etc.) or the like.

Suitable "protected hydroxy" may include "acyl" as mentioned below, phenyl(lower)alkyl which may have one or more suitable substituent(s) (e.g. benzyl, 4-methoxybenzyl, trityl, etc.), trisubstituted silyl [e.g., tri-(lower)alkylsilyl (e.g., trimethylsilyl, t-butyldimethylsilyl, etc.) etc.], tetrahydropyranyl, and the like.

Suitable "heterocyclic" moiety in the term of "heterocyclic group" and "heterocyclic(lower)alkyl" may include saturated or unsaturated, monocyclic or polycyclic heterocyclic group containing at least one hetero-atom such as an oxygen, sulfur, nitrogen atom, and the like, in which the preferred one may be

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.), tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-

membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s), for example, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, oxazolyl, isoxazolyl, oxadiazolyl (e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, morpholinyl, sydnonyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, benzoxazolyl, benzoxadiazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.), dihydrothiazinyl, etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolidinyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s), for example, thienyl, dihydrodithiinyl, dihydrodithionyl, etc.;

unsaturated condensed heterocyclic group containing 1

to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, benzothiazolyl, benzothiadiazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, furyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, dihydrooxathiinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s), for example, benzothienyl benzodithiinyl, etc.;

unsaturated condensed heterocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, benzoxathiinyl, etc.; and the like.

Suitable "lower alkyl" moiety in the term "aryloxy(lower)alkyl" and "ar(lower)alkyl" can be referred to aforementioned "lower alkyl".

Suitable "aryl" and "ar" moieties in the terms of "aryloxy(lower)alkyl", "arylamino(lower)alkyl", ar(lower)alkyl" and "ar(lower)alkoxy(lower)alkyl" may include phenyl, phenyl having lower alkyl (e.g., tolyl, xylyl, mesityl, cumenyl, etc.), naphthyl, anthryl, and the like, in which the preferred one may be (C_6-C_{10})aryl, and the most preferred one may be phenyl and naphthyl.

Suitable "ar(lower)alkyl" moiety may include benzyl, phenethyl, 1-(or 2- or 3-)phenylpropyl, 1-(or 2- or 3- or 4-)phenylbutyl, naphthylmethyl, naphthylethyl, 1-(or 2- or 3-)naphthylpropyl, naphthalene-1-yl-methyl, naphthalene-1-yl-ethyl, 1-(naphthalene-1-yl)propyl, 2-(naphthalene-1-yl)propyl, 3-(naphthalene-1-yl)propyl, and the like, in which the preferred one may be phenyl(C_1-C_3)alkyl and naphthyl(C_1-C_3)alkyl, and the most preferred one may be benzyl, phenethyl, 3-phenylpropyl and naphthalene-1-yl-methyl.

Suitable "lower alkoxy(lower)alkyl" moiety in the term of "ar(lower)alkoxy(lower)alkyl" may include methoxymethyl, 1-(or 2-)methoxyethyl, 1-(or 2- or 3-)-methoxypropyl, 1-(or 2- or 3- or 4-)methoxybutyl, 1-(or 2-)ethoxyethyl, 1-(or 2- or 3-)ethoxypropyl, 1-(or 2- or 3- or 4-)ethoxybutyl, 1-(or 2-)propoxyethyl, 1-(or 2- or 3-)propoxypropyl, 1-(or 2-)butoxyethyl, 1-(or 2- or 3-)-butoxypropyl, and the like.

Suitable "lower alkoxy" may be straight or branched one such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentyloxy, isopentyloxy, neopentyloxy, tert-pentyloxy, n-hexyloxy, or the like, in which the preferred one may be (C_1-C_4)alkoxy, and most preferred one may be methoxy and ethoxy.

Suitable "lower alkoxy(lower)alkoxy(lower)alkyl" may be methoxymethoxymethyl, methoxyethoxymethyl, methoxyethoxymethyl, methoxyethoxyethyl, ethoxymethoxymethyl, ethoxyethoxymethyl, ethoxyethoxyethyl, and the like, in which the most preferred one may be methoxyethoxyethyl.

Suitable "higher alkenyl which may have one or more suitable substituent(s)" may be 1-(or 2- or 3- or 4- or 5- or 6-)heptenyl, 1-(or 2- or 3- or 4- or 5- or 6- or 7-)-octenyl, 1-(or 2- or 3- or 4- or 5- or 6- or 7- or 8-)-nonanyl, 1,3-heptadienyl, 2,4-heptadienyl, 3,5-heptadienyl, and the like, in which the preferred one may be (C_7-C_9)alkenyl, and the most preferred one may be 2,4-heptadienyl.

Suitable "suitable substituent(s)" moiety in the term of "higher alkenyl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in which thew preferred one may be (C_1-C_4)alkyl, and the most preferred one may be methyl and ethyl.

Suitable "propoxypropyl" may be a straight or

branched one such as 1-(or 2- or 3-)n-propoxy-n-propyl, 1-(or 2-)n-propoxy-isopropyl, 1-(or 2- or 3-)isopropoxy-n-propyl, 1-(or 2-)isopropoxy-isopropyl, or the like.

Suitable "ethoxypropyl" may be a straight or branched one such as 1-(or 2- or 3-)ethoxy-n-propyl, 1-(or 2-)-ethoxy-isopropyl, or the like.

Suitable "butoxypropyl" may be a straight or branched one such as 1-(or 2- or 3-)n-butoxy-n-propyl, 1-(or 2- or 3-)isobutoxy-n-propyl, 1-(or 2- or 3-)sec-butoxy-n-propyl, 1-(or 2- or 3-)tert-butoxy-n-propyl, 1-(or 2-)n-butoxy-isopropyl, 1-(or 2-)isobutoxy-isopropyl, 1-(or 2-)sec-butoxy-isopropyl, 1-(or 2-)tert-butoxy-isopropyl, or the like.

Suitable "propoxyethyl" may be a straight or branched one such as 1-(or 2-)n-propoxyethyl, 1-(or 2-)-isopropoxyethyl, or the like.

Suitable "butoxyethyl" may be a straight or branched one such as 1-(or 2-)n-butoxyethyl, 1-(or 2-)-isobutoxyethyl, 1-(or 2-)sec-butoxyethyl, 1-(or 2-)tert-butoxyethyl, or the like.

Suitable "butoxybutyl" may be straight or branched one such as 1-(or 2- or 3- or 4-)n-butoxy-n-butyl, 1-(or 2- or 3- or 4-)isobutoxy-n-butyl, 1-(or 2- or 3- or 4-)-sec-butoxy-n-butyl, 1-(or 2- or 3- or 4-)tert-butoxy-n-butyl, 1-(or 2- or 3-)n-butoxy-isobutyl, 1-(or 2- or 3-)-sec-butoxy-isobutyl, 1-(or 2- or 3-)tert-butoxy-isobutyl, 1-(or 2- or 3-)n-butoxy-sec-butyl, 1-(or 2- or 3-)-isobutoxy-sec-butyl, 1-(or 2- or 3-)sec-butoxy-sec-butyl, or the like.

Suitable "methoxybutyl" may be a straight or branched one such as 1-(or 2- or 3- or 4-)methoxy-n-butyl, 1-(or 2- or 3-)methoxy-isobutyl, 1-(or 2- or 3-)methoxy-sec-butyl, or the like.

Suitable "ethoxybutyl" may be a straight or branched one such as 1-(or 2- or 3- or 4-)ethoxy-n-butyl, 1-(or 2-

or 3-)ethoxy-isobutyl, 1-(or 2- or 3-)ethoxy-sec-butyl, or the like.

Suitable "aryl" moiety in the term of "arylamino(lower)alkyl" can be referred to aforementioned "aryl".

Suitable "lower alkyl" moiety in the term of "arylamino(lower)alkyl" can be referred to aforementioned "lower alkyl".

Suitable "lower alkyl" moiety in the term of "pyridin-4-yl(lower)alkyl", "pyridin-3-yl(lower)alkyl", "lower alkyl-substituted pyridyl(lower)alkyl" and "imidazolyl(lower)alkyl" can be referred to aforementioned "lower alkyl".

Suitable "lower alkylene" may include straight or branched one such as methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, methylmethylene, ethylethylene, propylene, or the like, in which the preferred one may be (C_1-C_4)alkylene and the most preferred one may be methylene and ethylene.

Suitable "lower alkenylene" may include straight or branched one having 2 to 6 carbon atom(s) such as vinylene, propenylene, 1-(or 2-)butenylene, 1-(or 2- or 3-)pentenylene, 1-(or 2- or 3-)hexenylene, methylvinylene, ethylvinylene, 1-(or 2- or 3-)methylpropenylene, 1-(or 2- or 3-)ethylpropenylene, 1-(or 2- or 3- or 4-)methyl-1-(or 2-)butenylene, or the like, in which the preferred one may be (C_2-C_4)alkenylene, and the most preferred one may be vinylene and propenylene.

Suitable "unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s)" may be thienyl, thienylidene, dihydrodithiinyl, dihydrodithionyl, and the like, in which the preferred one may be 5 or 6-membered one, and the most preferred one may be thienyl.

Suitable "unsaturated 3 to 8-membered

heteromonocyclic group containing 1 to 2 oxygen atom(s)" in the term of "unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) which may have one or more suitable substituent(s)" may be furyl, furylidene, pyranyl, and the like, in which the preferred one may be 5 or 6-membered one, and the most preferred one may be furyl.

Suitable "unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atom(s)" may be indolyl, indolylidene, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, and the like, in which the preferred one may be indolyl and quinolyl.

Suitable "saturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s)" may be oxyranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyranylidene, dioxoranyl, dioxanyl, and the like, in which the preferred one may be 5 or 6-membered one, and the most preferred one may be dioxoranyl and tetrahydropyranyl and tetrahydropyranylidene.

Suitable "saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s)" may be pyrrolidinyl, imidazolidinyl, piperidyl, piperidylidene, piperazinyl, and the like, in which the preferred one may be 5 or 6-membered one, and the most preferred one may be piperidyl.

Suitable "unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s)" in the term of "unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) which may have one or more suitable substituent(s)" may be thiazolyl thiazolylidene, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.), dihydrothiazinyl, and the like,

in which the preferred one may be 5 or 6-membered one, and the most preferred one may be thiazolyl.

Suitable "acyl" moiety in the term of "acyl" and "acylamino" may include carbamoyl, aliphatic acyl group and acyl group containing an aromatic ring, which is referred to as aromatic acyl, or heterocyclic ring, which is referred to as heterocyclic acyl.

Suitable example of said acyl may be illustrated as follows :

Carbamoyl;

Aliphatic acyl such as lower or higher alkanoyl (e.g., formyl, acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, 2,2-dimethylpropanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl, icosanoyl, etc.);

lower or higher alkoxycarbonyl (e.g., methoxycarbonyl, ethoxycarbonyl, t-butoxycarbonyl, t-pentyloxycarbonyl, heptyloxycarbonyl, etc.);

lower or higher alkylsulfonyl (e.g., methylsulfonyl, ethylsulfonyl, etc.);

lower or higher alkoxysulfonyl (e.g., methoxysulfonyl, ethoxysulfonyl, etc.); or the like.

Aromatic acyl such as

aroyl (e.g. benzoyl, toluoyl, naphthoyl, etc.);

ar(lower)alkanoyl [e.g., phenyl(lower)alkanoyl (e.g., phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutanoyl, phenylpentanoyl, phenylhexanoyl, etc.), naphthyl(lower)alkanoyl (e.g., naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, etc.), etc.];

ar(lower)alkenoyl [e.g., phenyl(lower)alkenoyl (e.g., phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl, phenylhexenoyl, etc.), naphthyl(lower)alkenoyl (e.g., naphthylpropenoyl,

naphthylbutenoyl, etc.), etc.];
ar(lower)alkoxycarbonyl [e.g., phenyl(lower)alkoxycarbonyl (e.g. benzyloxycarbonyl, etc.), etc.];
aryloxycarbonyl (e.g., phenoxycarbonyl, naphthyloxycarbonyl, etc.);
aryloxy(lower)alkanoyl (e.g., phenoxyacetyl, phenoxypropionyl, etc.);
arylcarbamoyl (e.g., phenylcarbamoyl, etc.);
arylthiocarbamoyl (e.g., phenylthiocarbamoyl, etc.);
arylglyoxyloyl (e.g., phenylglyoxyloyl, naphthylglyoxyloyl, etc.);
arylsulfonyl (e.g., phenylsulfonyl, p-tolylsulfonyl, etc.); or the like;

Heterocyclic acyl such as
heterocycliccarbonyl;
heterocyclic(lower)alkanoyl (e.g., heterocyclicacetyl, heterocyclicpropanoyl, heterocyclicbutanoyl, heterocyclicpentanoyl, heterocyclichexanoyl, etc.);
heterocyclic(lower)alkenoyl (e.g., heterocyclicpropenoyl, heterocyclicbutenoyl, heterocyclicpentenoyl, heterocyclichexenoyl, etc.); heterocyclicglyoxyloyl; or the like;

in which suitable "heterocyclic moiety" in the terms "heterocycliccarbonyl", "heterocyclic(lower)alkanoyl", heterocyclic(lower)alkenoyl" and "heterocyclicglyoxyloyl" as mentioned above means, in more detail, saturated or unsaturated monocyclic or polycyclic heterocyclic group containing at least one hetero-atom such as an oxygen, sulfur, nitrogen atom and the like.

And, especially preferable heterocyclic group may be heterocyclic group such as

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl,

pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.), tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s), for example, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, oxazolyl, isoxazolyl, oxadiazolyl (e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, morpholinyl, sydnonyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, benzoxazolyl, benzoxadiazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.), dihydrothiazinyl, etc.;

saturated 3 to 8-memberd (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 2 nitrogen atom(s), for example, thiazolidinyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s), for example, thienyl, dihydrodithiinyl, dihydrodithionyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, benzothiazolyl, benzothiadiazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, furyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, dihydrooxathiinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s), for example, benzothienyl, benzodithiinyl, etc.;

unsaturated condensed heterocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, benzoxathiinyl, etc.; and the like,

in which the preferred one may be carbamoyl and Aliphatic acyl, and the more preferred one may be carbamoyl and lower alkanoyl, and the most preferred one may be carbamoyl and acetyl.

The acyl moiety as stated above may have one to ten, same or different, suitable substituent(s) such as lower alkyl (e.g., methyl, ethyl, propyl, etc.); lower alkoxy (e.g., methoxy, ethoxy, propoxy, etc.); lower alkylthio (e.g., methylthio, ethylthio, etc.); lower alkylamino (e.g., methylamino, ethylamino, propylamino, etc.); cyclo(lower)alkyl (e.g., cyclopentyl, cyclohexyl, etc.); cyclo(lower)alkenyl (e.g., cyclohexenyl, cyclohexadienyl, etc.); halogen (e.g., fluorine, chlorine, bromine, iodine); amino, protected amino as mentioned above; hydroxy; protected hydroxy as mentioned above; cyano;

nitro; carboxy; protected carboxy as mentioned above; sulfo; sulfamoyl; imino; oxo; amino(lower)alkyl (e.g., aminomethyl, aminoethyl, etc.); carbamoyloxy; hydroxy(lower)alkyl (e.g., hydroxymethyl, 1 or 2-hydroxyethyl, 1 or 2 or 3-hydroxypropyl, etc.), or the like.

Suitable "acid residue" may include halogen (e.g., fluorine, chlorine, bromine, iodine), acyloxy [e.g., sulfonyloxy (e.g., phenylsulfonyloxy, tosyloxy, mesyloxy, etc.), lower alkanoyloxy (e.g., acetyloxy, propionyloxy, etc.), etc.], and the like.

Suitable pharmaceutically acceptable salts of the object compound (I) are conventional non-toxic salts and include an organic acid addition salt [e.g. formate, acetate, trifluoroacetate, maleate, tartrate, oxalate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.], an inorganic acid addition salt [e.g. hydrochloride, hydrobromide, sulfate, phosphate, etc.], a salt with an acidic amino acid [e.g. aspartic acid salt, glutamic acid salt, etc.], and the like.

With respect to the salt of the compound (Ia) to (Ib) in the Processes 1 to 4, it is to be noted that these compounds are included within the scope of the compound (I), and accordingly the suitable examples of the salts of those compounds are to be referred to those as exemplified for the object compound (I).

The processes for preparing the object compound (I) of the present invention are explained in detail in the following.

Process 1

The object compound (I) or a salt thereof can be

prepared by reacting the compound (II) or a salt thereof with the compound (III) or a salt thereof.

This reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as alcohol [e.g. methanol, ethanol, propanol, etc.], tetrahydrofuran, dioxane, dimethyl sulfoxide, N,N-dimethylformamide or a mixture thereof.

In case that the compound (III) is liquid, it can be also used as a solvent.

The reaction temperature is not critical, and the reaction is usually carried out at ambient temperature or under warming or heating.

Process 2

The object compound (Ib) or a salt thereof can be prepared by subjecting the compound (Ia) or a salt thereof to deacylation.

Suitable method for this deacylation reaction may include conventional one such as hydrolysis, reduction or the like. The hydrolysis is preferably carried out in the presence of a base or an acid.

Suitable base may include, for example, an inorganic base such as alkali metal hydroxide (e.g. sodium hydroxide, potassium hydroxide, etc.), alkaline earth metal hydroxide (e.g. magnesium hydroxide, calcium hydroxide, etc.), alkali metal carbonate (e.g. sodium carbonate, potassium carbonate, etc.), alkaline earth metal carbonate (e.g. magnesium carbonate, calcium carbonate, etc.), alkali metal bicarbonate (e.g. sodium bicarbonate, potassium bicarbonate, etc.), alkali metal acetate (e.g. sodium acetate, potassium acetate, etc.), alkaline earth metal phosphate (e.g. magnesium phosphate, calcium phosphate, etc.), alkali metal hydrogen phosphate (e.g. disodium hydrogen phosphate, dipotassium hydrogen phosphate, etc.), or the like, and an organic base such as

tri-(lower)alkylamine (e.g. trimethylamine, triethylamine, etc.), picoline, N-methylpyrrolidine, N-methylmorpholine, 1,5-diazabicyclo[4.3.0]non-5-one, 1,4-diazabicyclo[2,2,2]-octane, 1,5-diazabicyclo[5,4,0]undecene-5 or the like.

The hydrolysis using a base is often carried out in water or a hydrophilic organic solvent or a mixed solvent thereof.

Suitable acid may include an organic acid (e.g. formic acid, acetic acid, propionic acid, etc.) and an inorganic acid (e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, etc.).

The present hydrolysis is usually carried out in an organic solvent such as alcohol (e.g. methanol, ethanol, etc.), water or a mixed solvent thereof.

The reaction temperature is not critical, and the reaction is usually carried out at ambient temperature or under warming or heating.

Process 3

The object compound (I) or a salt thereof can be prepared by reacting the compound (Ib) or a salt thereof with an acylating agent.

The compound (Ib) may be used in the form of its conventional reactive derivative at the amino group.

The acylating agent can be represented by the compound of the formula :

$$R^6 - OH$$

in which R^6 is acyl as defined above and its conventional reactive derivative at the hydroxy group, or a salt thereof.

The suitable example may be an acid halide (e.g. acid chloride, etc.), an acid anhydride, an activated amide, an activated ester, and the like.

In case the acyl group to be introduced is a

carbamoyl type acyl, the acylating agent is usually used in the form of cyanate or isocyanate.

The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, etc.] acetone, dioxane, acetonitrile, chloroform, dichloromethane, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, N,N-dimethylacetamide, pyridine, acetic acid or any other organic solvent which does not adversely influence the reaction. These conventional solvents may also be used in a mixture with water.

The reaction temperature is not critical, and the reaction is usually carried out under cooling to warming.

The reaction may also be carried out in the presence of an inorganic or organic base such as an alkali metal bicarbonate, tri-(lower)alkylamine, pyridine, N-(lower)-alkylmorphorine, N,N-di-(lower)alkylbenzylamine, or the like.

Process 4

The object compound (I) or a salt thereof can be prepared by reacting the compound (IV) or a salt thereof with the compound (V) or a salt thereof.

This reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as ethyl acetate, dichloromethane, chloroform, carbon tetrachloride, tetrahydrofuran, N,N-dimethylformamide, N,N-dimethylacetamide, acetonitrile, dioxane, water, alcohol [e.g. methanol, ethanol, etc.] acetic acid, formic acid, etc. or a mixture thereof.

The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

The processes for preparing the compound (V) of the present invention are explained in detail in the

following.

Process A

The object compound (V) or a salt thereof can be prepared by reacting the compound (VI) or a salt thereof with the compound (III) or a salt thereof.

This reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as alcohol [e.g. methanol, ethanol, propanol, etc.], tetrahydrofuran, dioxane, dimethyl sulfoxide, N,N-dimethylformamide or a mixture thereof.

In case that the compound (III) is liquid, it can be also used as a solvent.

This reaction is preferably carried out in the presence of an acid.

Suitable acid may include, for example, an organic acid (e.g. formic acid, acetic acid, propionic acid, p-toluenesulfonic acid, etc.) and an inorganic acid (e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, ammonium chloride, etc.).

The reaction temperature is not critical, and the reaction is usually carried out at ambient temperature or under warming or heating.

Process B

The object compound (V) or a salt thereof can be prepared by reacting the compound (VII) or a salt thereof with the compound (III) or a salt thereof.

This reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as alcohol [e.g. methanol, ethanol, propanol, etc.], tetrahydrofuran, dioxane, dimethyl sulfoxide, N,N-dimethylformamide or a mixture thereof.

In case that the compound (III) is liquid, it can be also used as a solvent.

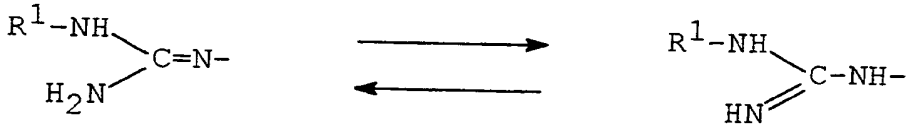
The reaction temperature is not critical, and the reaction is usually carried out at ambient temperature or under warming or heating.

Among the starting compounds, some of them are new and such compounds can be prepared by the methods of Preparations mentioned below and by any process known in the art for preparing structurally analogous compounds thereto.

The compounds obtained by the above Processes 1 to 4 can be isolated and purified by a conventional method such as pulverization, recrystallization, column chromatography, reprecipitation or the like.

It is to be noted that each of the object compound (I) may include one or more stereoisomer such as optical isomer(s) and geometrical isomer(s) due to asymmetric carbon atom(s) and double bond(s) and all such isomers and mixture thereof are included within the scope of this invention.

Furthermore, with regard to the compound (I) it is to be noted that the following formula (A) is well known to lie to tautomeric relation with the following formula (B), and accordingly, it is to be understood that both of the isomers are substantially the same.



(A) (B)

Accordingly, the both of the tautomeric forms are clearly included within the scope of the present invention. In the present specification, the object and starting compounds including the group of such tautomeric isomers are represented by using one of the expressions.

The new furylthiazole derivatives (I) and

pharmaceutically acceptable salts thereof possess antiulcer activity and H_2-receptor antagonism, and are useful for a therapeutic treatment and/or prevention of gastritis, ulcer (e.g. gastric ulcer, duodenal ulcer, anastomotic ulcer, etc.), Zollinger-Ellison syndrome, reflux esophagitis, upper gastrointestinal bleeding, and the like.

And further, the compound (I) and pharmaceutically acceptable salts thereof of the present invention possess high antimicrobial activity against pathogenic microorganisms such as helicobacter pylori (campylobactor pyloridis), and the like, which is a gram-negative bacillus that has recently been found beneath the mucus gel of the human stomach.

For therapeutic purpose, the compound (I) and a pharmaceutically acceptable salt thereof of the present invention can be used in a form of pharmaceutical preparation containing one of said compounds, as an active ingredient, in admixture with a pharmaceutically acceptable carrier such as an organic or inorganic solid or liquid excipient suitable for oral or parenteral administration. The pharmaceutical preparations may be capsules, tablets, dragees, granules, solution, suspension, emulsion, or the like. If desired, there may be included in these preparations, auxiliary substances, stabilizing agents, wetting or emulsifying agents, buffers and other commonly used additives.

While the dosage of the compound (I) will vary depending upon the age and condition of the patient, an average single dose of about 0.1 mg, 1 mg, 10 mg, 50 mg, 100 mg, 250 mg, 500 mg and 1000 mg of the compound (I) may be effective for treating ulcer. In general, amounts, between 0.1 mg/body and about 1,000 mg/body may be administered per day.

In order to illustrate the usefulness of the object compound (I), the pharmacological test data of some representative compounds of the compound (I) are shown in the following.

Test Compound

(1) 4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-phenylpropylamino)methyleneamino]thiazole

(2) 4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(cyclohexylethylamino)methyleneamino]thiazole

Test A (Inhibition of HCl-aspirin ulcer) :

Test Method

Seven male Sprague-Dawley rats, aged 6 weeks and weighing about 200 g were used per group for the study on HCl-aspirin ulcer after the fast for 24 hours. Each of the test compounds (32 mg/kg) suspended in 0.1% methylcellulose solution was administered orally 30 minutes before aspirin administration. Aspirin, suspended in 0.1% methylcellulose solution containing 0.2N HCl, was administered orally at a dose of 200 mg/kg/10 ml. One hour later, the animals were sacrificed and their stomachs were removed. The stomach was then fixed with 2% formalin. The length of ulcers was measured for each animal, and percentage of inhibition was calculated by comparing the mean length of ulcers (mm) in the test animals with that in the control animals.

Test Result

Test Compound	Inhibition (%)
(1)	77.9

Test Compound	Inhibition (%)
(1)	77.9

Test B (Anti-microbial activity) :

Test Method

In vitro antimicrobial activity was determined by the agar dilution method. Test strain was precultured in Brucella broth containing 5% horse serum at 37°C for 3 days and 10^4 cfu/ml were inoculated with a multipoint replicater onto Brucella agar plus 5% lysed horse blood plate containing serial 2-fold dilutions of each drug at 37°C for 3 days. Incubation was carried out in an atmosphere of 10% CO_2. MIC was read after incubation as the lowest drug concentration that inhibited macroscopic colonial growth.

Test Result

MIC (μg/ml)

Test Compound / Test strain	(2)
helicobacter pylori 8008	< 0.2

The following Preparations and Examples are given for the purpose of illustrating the present invention in more detail.

Preparation 1

A mixture of 3-[(amino)(methylthio)methylene]thiourea hydroiodide (7.0 g), 2-chlorobenzylamine (14.1 g) in ethanol (50 ml) was refluxed for 3 hours. The reaction mixture was evaporated in vacuo. The residue was diluted with 2N-hydrochloric acid (20 ml), and washed with ethyl acetate. The aqueous layer was saturated with sodium chloride and extracted with ethyl acetate. The extract was washed with brine, dried over anhydrous sodium sulfate, and evaporated in vacuo. The residue was recrystallized from a mixture of ethyl acetate and diethyl ether to give N-[(amino)(2-chlorobenzylamino)methylene]-thiourea (4.90 g).

m.p.: 176-178°C

IR (Nujol) : 3300, 3150, 1700, 1640, 1600 cm^{-1}

NMR (DMSO-d_6, δ) : 4.68 (2H, d, J=4.5Hz), 7.36-7.55 (4H, m), 8.75 (1H, br s), 9.23-9.32 (3H, m), 10.06 (1H, br s), 11.85 (1H, br s)

Preparation 2

A mixture of N-(diaminomethylene)thiourea (20.6 g) and 2-methoxyphenethylamine (52.7 g) in acetic acid (30 ml) and ethanol (100 ml) was refluxed for 22 hours. To the reaction mixture was added ethanol (80 ml) and water (720 ml). The resulting precipitate was collected by filtration. The obtained residue was mixed with water. The mixture was adjusted to pH=8.5 with 20% potassium carbonate aqueous solution and extracted with ethyl acetate. The extract was washed with brine, dried over anhydrous magnesium sulfate, and evaporated in vacuo. The residual oil was crystallized from a mixture of ethyl acetate and diisopropyl ether to give N-[(amino)(2-methoxyphenethylamino)methylene]thiourea (13.2 g).

m.p.: 102-103°C

IR (Nujol) : 3460, 3325, 1645, 1620 cm^{-1}

NMR (DMSO-d_6, δ) : 2.75 (2H, t, J=7.5Hz), 3.25-3.35 (2H, m), 3.79 (3H, s), 6.88 (1H, t, J=7.4Hz), 6.96 (1H, d, J=7.4Hz), 7.00 (4H, br s), 7.19 (1H, d, J=7.4Hz), 7.21 (1H, t, J=7.4Hz), 7.90 (1H, br s)

The following compound was obtained according to a similar manner to that of Preparation 1.

Preparation 3

N-[(Amino)(4-chloroanilino)methylene]thiourea

IR (Nujol) : 3350, 1655, 1500 cm-1

NMR (DMSO-d_6, δ) : 5.88 (1H, br s), 6.88 (1H, d, J=8.1Hz), 7.30 (2H, d, J=8.3Hz), 7.49-7.70 (2H, m), 8.30 (1H, br s), 9.06 (1H, br s), 9.47 (1/2H, br s), 10.73 (1/2H, br s)

Preparation 4

To a solution of dimethylamine (5.4 g) in dichloromethane (30 ml) was added dropwise 2-cyanobenzenesulfonyl chloride (5 g) in dichloromethane (30 ml) at 5°C and then stirred for 2 hours at room temperature. After removed of the solvent, the residue was dissolved in a mixture of water (30 ml) and ethyl acetate (30 ml) and then extracted with ethyl acetate. The extract was washed with water and brine, dried over sodium sulfate and then evaporated in vacuo. The residue was crystallized from ethyl acetate and diethyl ether to give 2-(N,N-dimethylsulfamoyl)benzonitrile.

m.p. : 52-53°C

IR (Nujol) : 2230, 1170 cm^{-1}

NMR (DMSO-d_6, δ) : 2.78 (6H, s), 7.86-8.20 (4H, m)

Preparation 5

To a solution of phenol (2 g) in N,N-

dimethylformamide (20 ml) was added portionwise sodium hydride (60% oil suspension) (800 mg) for 5 minutes at 10°C, and then stirred for 10 minutes at room temperature. 2-Bromomethylbenzonitrile (3.98 g) was added portionwise to the resultant mixture at 10°C, and then stirred for 2 hours at room temperature. The reaction mixture was diluted with n-hexane (30 ml). Resulting precipitate was collected by filtration to give 2-phenoxymethyl-benzonitrile.

m.p. : 64-65°C

IR (Nujol) : 2230, 1595, 1580, 1495 cm^{-1}

NMR (DMSO-d_6, δ) : 5.25 (2H, s), 6.34-7.08 (3H, m), 7.25-7.38 (2H, m), 7.55-7.63 (1H, m), 7.70-7.78 (2H, m), 7.91 (1H, d, J=7.5Hz)

Preparation 6 (1)

To a suspension of lithium aluminum hydride (45.5 mg) in diethyl ether (5 ml) was added dropwise 2-(N,N-dimethylsulfamoyl)benzonitrile (210 mg) in diethyl ether (5 ml) at 10°C. The resultant mixture was stirred for 1 hour at room temperature and then aqueous solution of potassium sodium tartrate (2 ml) was added to that mixture at 5°C. Organic layer was separated by decantation and then dried over sodium sulfate and evaporated in vacuo to give 2-(N,N-dimethylsulfamoyl)benzylamine.

m.p. : 49-51°C

IR (Nujol) : 3230, 3120, 1640, 1580, 1550, 1530, 1320, 1150 cm^{-1}

NMR (DMSO-d_6, δ) : 2.72 (6H, s), 4.01 (2H, s), 7.40-7.81 (4H, m)

The following compound was obtained according to a similar manner to that of Preparation 6 (1).

Preparation 6 (2)

2-Phenoxymethylbenzylamine

m.p. : 145-147°C

IR (Nujol) : 3350, 1600, 1585, 1495 cm^{-1}

NMR ($CDCl_3$, δ) : 1.57 (2H, br s), 3.97 (2H, s), 5.11 (2H, s), 6.88-7.05 (4H, m), 7.16-7.50 (5H, m)

Example 1 (1)

A suspension of 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(methylthio)methyleneamino]thiazole hydroiodide (6.57 g) and cyclohexylmethylamine (8.49 g) in ethanol (50 ml) was refluxed for 72 hours. The reaction mixture was evaporated in vacuo. The residue was diluted with ethyl acetate. The resulting precipitate was filtered off. The filtrate was washed with water and brine, dried over anhydrous magnesium sulfate, and evaporated in vacuo. The residue was purified by chromatography on silica gel eluting with (4% methanol/chloroform) to give 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)-(cyclohexylmethylamino)methyleneamino]thiazole (5.08 g).

m.p.: 183-184°C

IR (Nujol) : 3300, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.95-1.02 (2H, m), 1.13-1.35 (4H, m), 1.40-1.77 (5H, m), 1.85 (3H, s), 3.03 (2H, t, J=6.0Hz), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.53 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.24 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{18}H_{25}N_5O_2S \cdot 1/4H_2O$:

C 56.90; H 6.76; N 18.43

Found : C 56.94; H 6.84; N 18.14

The following compounds were obtained according to a similar manner to that of Example 1 (1).

Example 1 (2)

4-(5-Acetylaminomethylfuran-2-yl)-2-

[(amino)(isopropylamino)methyleneamino]thiazole

m.p.: 104-105°C

IR (Nujol) : 3440, 3200, 1620 cm^{-1}

NMR (DMSO-d_6, δ) : 1.13 (6H, d, J=6.4Hz), 1.86 (3H, s), 3.81-3.91 (1H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.33 (2H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{14}H_{19}N_5O_2S \cdot H_2O$:

C 49.54; H 6.24; N 20.63

Found : C 49.31; H 6.37; N 20.55

Example 1 (3)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methylpropylamino)methyleneamino]thiazole

IR (Nujol) : 3250, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.92 (6H, d, J=6.7Hz), 1.70-1.82 (1H, m), 1.86 (3H, s), 3.01 (2H, t, J=6.1Hz), 4.26 (2H, d, J=5.5Hz), 6.23 (1H, d, J=3.1Hz), 6.54 (1H, d, J=3.1Hz), 6.77 (1H, s), 7.26 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Example 1 (4)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methylbutylamino)methyleneamino]thiazole

m.p.: 167-168°C

IR (Nujol) : 3300, 1660 cm^{-1}

NMR (DMSO-d_6, δ) : 0.89 (3H, t, J=7.3Hz), 0.91 (3H, d, J=6.5Hz), 1.06-1.23 (1H, m), 1.37-1.60 (2H, m), 1.85 (3H, s), 2.95-3.18 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.25 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{16}H_{23}N_5O_2S$:

C 54.99; H 6.63; N 20.04

Found : C 54.62; H 6.72; N 19.75

Example 1 (5)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-methylbutylamino)methyleneamino]thiazole

IR (Neat) : 3250, 1620 cm^{-1}

NMR (DMSO-d_6, δ) : 0.91 (6H, d, J=6.5Hz), 1.41 (2H, q, J=6.5Hz), 1.55-1.76 (1H, m), 1.87 (3H, s), 3.10-3.23 (2H, m), 4.28 (2H, d, J=5.5Hz), 6.32 (1H, d, J=3.2Hz), 6.58 (1H, d, J=3.2Hz), 6.86 (1H, s), 7.49 (3H, br s), 8.37 (1H, t, J=5.5Hz)

Example 1 (6)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2,2-dimethylpropylamino)methyleneamino]thiazole

m.p.: 119-120°C

IR (Nujol) : 3200, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 0.95 (9H, s), 1.85 (3H, s), 3.05 (2H, d, J=5.7Hz), 4.26 (2H, d, J=5.5Hz), 6.31 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.86 (1H, s), 7.30 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{16}H_{23}N_5O_2S \cdot H_2O$:

C 52.30; H 6.86; N 19.06

Found : C 52.55; H 6.85; N 18.97

Example 1 (7)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(n-heptylamino)methyleneamino]thiazole

m.p.: 129-131°C

IR (Nujol) : 3300, 1645 cm^{-1}

NMR (DMSO-d_6, δ) : 0.86 (3H, t, J=6.7Hz), 1.20-1.50 (8H, m), 1.40-1.60 (2H, m), 3.20-3.40 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.28 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.32 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Example 1 (8)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(n-octylamino)methyleneamino]thiazole

IR (Nujol) : 3450, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 0.85 (3H, t, J=6.6Hz), 1.25 (10H, br s), 1.40-1.60 (2H, m), 1.85 (3H, s), 3.15 (2H, q, J=6.6Hz), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.31 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Example 1 (9)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(methylthio)ethylamino}methyleneamino]thiazole

m.p.: 138-139°C

IR (Nujol) : 3300, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.10 (3H, s), 2.63 (2H, t, J=6.7Hz), 3.32-3.43 (2H, m), 4.27 (2H, d, J=5.4Hz), 6.30 (1H, d, J=3.2Hz), 6.62 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.45 (3H, br s), 8.35 (1H, t, J=5.4Hz)

Anal Calcd. for $C_{14}H_{19}N_5O_2S_2$:

C 47.57; H 5.42; N 19.82

Found : C 47.52; H 5.38; N 19.95

Example 1 (10)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){(furan-2-yl)methylamino}methyleneamino]thiazole

m.p.: 182-183°C

IR (Nujol) : 3300, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 4.27 (2H, d, J=5.4Hz), 4.41 (2H, d, J=5.4Hz), 6.20-6.30 (2H, m), 6.42 (1H, dd, J=1.9 and 3.2Hz), 6.58 (1H, d, J=3.2Hz), 6.82 (1H, s), 7.50 (3H, br s), 7.61 (1H, d, J=1.9Hz), 8.35 (1H, t, J=5.4Hz)

Anal Calcd. for $C_{16}H_{17}N_5O_3S$:

C 53.47; H 4.77; N 19.49
Found : C 53.73; H 4.80; N 19.20

Example 1 (11)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(furan-2-yl)ethylamino}methyleneamino]thiazole

m.p.: 134-135°C

IR (Nujol) : 3300, 1655 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.85 (2H, t, J=6.9Hz), 3.40-3.70 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.20 (1H, d, J=3.1Hz), 6.30 (1H, d, J=3.1Hz), 6.38 (1H, dd, J=1.9 and 3.1Hz), 6.56 (1H, d, J=3.1Hz), 6.79 (1H, s), 7.45 (3H, br s), 7.54 (1H, d, J=1.9Hz), 8.36 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{19}N_5O_3S$:
C 54.68; H 5.13; N 18.76
Found : C 54.45; H 5.01; N 18.36

Example 1 (12)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-thienyl)ethylamino}methyleneamino]thiazole

m.p.: 163-164°C

IR (Nujol) : 3450, 3200, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.03 (2H, t, J=6.9Hz), 3.45 (2H, q, J=6.9Hz), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.79 (1H, s), 6.90-7.00 (2H, m), 7.35 (1H, dd, J=1.5 and 4.8Hz), 7.46 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{19}N_5O_2S_2$:
C 52.42; H 4.92; N 17.98
Found : C 52.28; H 4.95; N 17.96

Example 1 (13)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-

(imidazol-4-yl)ethylamino}methyleneamino]thiazole

m.p.: 189-191°C

IR (Nujol) : 3400, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.74 (2H, t, J=6.9Hz), 3.40-3.50 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.77 (1H, s), 6.89 (1H, s), 7.41 (3H, br s), 7.63 (1H, s), 8.37 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{16}H_{19}N_7O_2S \cdot 1/2H_2O$:

C 50.25; H 5.27; N 25.64

Found : C 50.56; H 5.19; N 25.35

Example 1 (14)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(pyridin-4-yl)ethylamino}methyleneamino]thiazole

m.p.: 237-239°C

IR (Nujol) : 3370, 1640, 1600, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.87 (3H, s), 2.85 (2H, t, J=6.9Hz), 3.45-3.55 (2H, m), 4.29 (2H, d, J=5.5Hz), 6.31 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.80 (1H, s), 7.30 (2H, d, J=5.9Hz), 7.47 (2H, br s), 8.37 (1H, t, J=5.5Hz), 8.48 (1H, dd, J=1.5 and 5.9Hz)

MASS (m/z) : 385 (M^++1)

Anal Calcd. for $C_{18}H_{20}N_6O_2S$:

C 56.23; H 5.24; N 21.86

Found : C 56.18; H 5.44; N 21.46

Example 1 (15)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-chlorophenethylamino)methyleneamino]thiazole

m.p.: 159-160°C

IR (Nujol) : 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.81 (2H, t, J=7.0Hz), 3.30-3.50 (2H, m), 4.27 (2H, d,

J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.50 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.24-7.50 (7H, m), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{20}ClN_5O_2S$:
C 54.60; H 4.82; N 16.76
Found : C 54.29; H 4.87; N 16.43

Example 1 (16)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-chlorophenethylamino)methyleneamino]thiazole

m.p.: 149-150°C

IR (Nujol) : 3300, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.83 (2H, t, J=7.0Hz), 3.40-3.50 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.2-7.3 (4H, m), 7.34 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Example 1 (17)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-methylphenethylamino)methyleneamino]thiazole

m.p.: 173-174°C

IR (Nujol) : 3300, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.26 (3H, s), 2.77 (2H, t, J=7.0Hz), 3.35-3.45 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.50 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.10 (2H, d, J=8.2Hz), 7.16 (2H, d, J=8.2Hz), 7.39 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_2S$:
C 60.43; H 5.83; N 17.62
Found : C 60.60; H 5.83; N 17.41

Example 1 (18)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-

methoxyphenethylamino)methyleneamino]thiazole

m.p.: 147-148°C

IR (Nujol) : 3325, 1655 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.75 (2H, t, J=7.1Hz), 3.30-3.50 (2H, m), 3.72 (3H, s), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.50 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.86 (2H, d, J=8.6Hz), 7.19 (2H, d, J=8.6Hz), 7.37 (3H, br s), 8.36 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_3S$:
C 58.09; H 5.61; N 16.94
Found : C 58.13; H 5.61; N 16.81

Example 1 (19)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-sulfamoylphenethylamino)methyleneamino]thiazole oxalate

m.p.: 212-214°C

IR (Nujol) : 3250, 1650, 1340, 1160 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.95 (2H, m), 3.50-3.60 (2H, m), 4.28 (2H, d, J=5.5Hz), 6.33 (1H, d, J=3.2Hz), 6.64 (1H, d, J=3.2Hz), 6.99 (1H, s), 7.31 (2H, s), 7.49 (2H, d, J=8.2Hz), 7.76 (2H, d, J=3.2Hz), 8.03 (3H, br s), 8.39 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{22}N_6O_4S_2 \cdot C_2H_2O_4 \cdot 1/2H_2O$:
C 44.91; H 4.49; N 14.96
Found : C 44.92; H 4.21; N 14.82

Example 1 (20)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-nitrophenethylamino)methyleneamino]thiazole

m.p.: 180-181°C

IR (Nujol) : 3350, 1650, 1540, 1340 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.97 (2H, t, J=7.1Hz), 3.50-3.60 (2H, m), 4.26 (2H, d,

J=5.6Hz), 6.28 (1H, d, J=3.3Hz), 6.50 (1H, d, J=3.3Hz), 6.79 (1H, s), 7.44 (3H, br s), 7.56 (2H, d, J=8.7Hz), 8.18 (2H, d, J=8.7Hz), 8.35 (1H, t, J=5.6Hz)

Example 1 (21)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-phenylpropylamino)methyleneamino]thiazole

m.p.: 117-118°C

IR (Nujol) : 3300, 2650, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.65 (2H, t, J=7.5Hz), 3.10-3.20 (2H, m), 3.3-3.5 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.0Hz), 6.57 (1H, d, J=3.0Hz), 6.78 (1H, s), 7.2-7.3 (5H, m), 7.39 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_2S$:
C 60.43; H 5.83; N 17.62
Found : C 60.32; H 5.70; N 17.50

Example 1 (22)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methoxyphenethylamino)methyleneamino]thiazole

m.p.: 151-152°C

IR (Nujol) : 3450, 3300, 1625 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.80 (2H, t, J=7.0Hz), 3.32-3.42 (2H, m), 3.80 (3H, s), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.50 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.89-6.99 (2H, m), 7.19 (2H, d, J=7.3Hz), 7.36 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_3S$:
C 58.09; H 5.61; N 16.94
Found : C 58.39; H 5.62; N 16.69

Example 1 (23)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(phenethylamino)methyleneamino]thiazole

m.p.: 100-102°C

IR (Nujol) : 3450, 3320, 1655, 1635, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.82 (2H, t, J=7.3Hz), 3.34-3.48 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.16-7.31 (5H, m), 7.41 (2H, br s), 8.35 (1H, t, J=5.5Hz)

MASS (m/z) : 384 (M^++1)

Anal Calcd. for $C_{19}H_{21}N_5O_2S$:

C 59.51; H 5.68; N 18.26

Found : C 59.42; H 5.62; N 18.02

Example 1 (24)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3,4-dimethoxyphenethylamino)methyleneamino]thiazole

m.p.: 135-138°C

IR (Nujol) : 3270, 1655, 1630, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.75 (2H, t, J=6.9Hz), 3.36-3.46 (2H, m), 3.71 (3H, s), 3.73 (3H, s), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.50 (1H, d, J=3.2Hz), 6.76-6.89 (3H, m), 7.38 (2H, br s), 8.35 (1H, t, J=5.5Hz)

MASS (m/z) : 444 (M^++1)

Anal Calcd. for $C_{21}H_{25}N_5O_4S$:

C 56.93; H 5.29; N 14.86

Found : C 56.77; H 6.10; N 14.46

Example 1 (25)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){4-(butoxy)butylamino}methyleneamino]thiazole oxalate

m.p.: 164°C (dec.)

IR (Nujol) : 3270, 1755, 1680 cm^{-1}

NMR (DMSO-d_6, δ) : 0.86 (3H, t, J=7.2Hz), 1.21-1.50

(4H, m), 1.59 (4H, br s), 1.86 (3H, s), 3.29-3.38 (6H, m), 4.28 (2H, d, J=5.5Hz), 6.33 (1H, d, J=3.2Hz), 6.70 (1H, d, J=3.2Hz), 7.07 (1H, s), 8.37 (1H, t, J=5.5Hz)

MASS (m/z) : 408 (M^++1) free of compound

Example 1 (26)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){3-(ethoxy)propylamino}methyleneamino]thiazole

m.p.: 155-156°C

IR (Nujol) : 3300, 3100, 1660, 1600, 1540, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.13 (3H, t, J=7.0Hz), 1.73 (2H, q, J=7.0Hz), 1.86 (3H, s), 3.16-3.27 (2H, m), 3.37-3.47 (4H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.4 (2H, br s), 8.35 (1H, t, J=5.5Hz)

MASS (m/z) : 366 (M^++1)

Anal Calcd. for $C_{16}H_{27}N_5O_3S$:

C 52.59; H 6.34; N 19.16

Found : C 52.56; H 6.63; N 18.99

Example 1-(27)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){4-(methoxy)butylamino}methyleneamino]thiazole oxalate

m.p.: 155-157°C

IR (Nujol) : 3270, 1775, 1660, 1630, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.59 (4H, s), 1.86 (3H, s), 3.23 (3H, s), 3.23-3.25 (4H, m), 4.28 (2H, d, J=5.4Hz), 6.34 (1H, d, J=7.2Hz), 6.72 (1H, d, J=3.2Hz), 7.09 (1H, s), 8.37 (1H, t, J=5.4Hz), 8.37 (2H, br s)

MASS (m/z) : 366 (M^++1) free of compound

Anal Calcd. for $C_{18}H_{25}N_5O_7S$:

C 47.47; H 5.53; N 15.38

Found : C 47.11; H 5.79; N 15.14

Example 1 (28)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(butoxy)ethylamino}methyleneamino]thiazole oxalate

m.p.: 178-179°C

IR (Nujol) : 3400, 1750, 1670, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 0.85 (3H, t, J=7.2Hz), 1.22-1.53 (4H, m), 1.86 (3H, s), 3.41-3.55 (6H, m), 4.28 (2H, d, J=5.3Hz), 4.06 (4H, br s), 6.32 (1H, d, J=3.1Hz), 6.69 (1H, d, J=3.1Hz), 7.04 (1H, s), 8.13 (1H, br s), 8.37 (1H, t, J=5.3Hz)

MASS (m/z) : 380 (M^++1) free of compound

Anal Calcd. for $C_{19}H_{27}N_5O_7S$:

C 48.61; H 5.80; N 14.92

Found : C 48.80; H 5.92; N 14.85

Example 1 (29)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(propoxy)ethylamino}methyleneamino]thiazole

m.p.: 142-143°C

IR (Nujol) : 3300, 3100, 1675, 1650, 1600 cm^{-1}

NMR (DMSO-d_6, δ) : 0.87 (3H, t, J=7.4Hz), 1.44-1.62 (2H, m), 1.85 (3H, s), 3.31-3.51 (6H, m), 4.26 (2H, d, J=5.4Hz), 6.29 (1H, d, J=3.2Hz), 6.59 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.39 (2H, br s), 8.35 (1H, t, J=5.4Hz)

MASS (m/z) : 366 (M^++1)

Anal Calcd. for $C_{16}H_{23}N_5O_3S$:

C 52.59; H 6.34; N 19.16

Found : C 52.43; H 6.46; N 19.04

Example 1 (30)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){4-(ethoxy)butylamino}methyleneamino]thiazole oxalate

m.p.: 135-136°C

IR (Nujol) : 3300, 1635, 1505 cm^{-1}

NMR (DMSO-d_6, δ) : 1.10 (3H, t, J=6.9Hz), 1.59 (4H, m), 1.86 (3H, s), 3.27-3.46 (6H, m), 4.28 (2H, d, J=5.4Hz), 6.33 (1H, d, J=3.1Hz), 6.72 (1H, d, J=3.1Hz), 7.08 (1H, s), 8.37 (1H, t, J=5.4Hz)

MASS (m/z) : 380 (M^++1) free of compound

Anal Calcd. for $C_{19}H_{27}N_5O_7S$:

C 48.61; H 5.80; N 14.92

Found : C 48.86; H 5.91; N 14.86

Example 1 (31)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){3-(butoxy)propylamino}methyleneamino]thiazole

m.p.: 137-138°C

IR (Nujol) : 3250, 3100, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 0.87 (3H, t, J=7.3Hz), 1.31 (2H, q, J=7.3Hz), 1.48 (2H, q, J=6.7Hz), 1.73 (2H, q, J=6.7Hz), 1.85 (3H, s), 3.25 (2H, q, J=6.7Hz), 3.3-3.4 (2H, m), 3.41 (2H, q, J=6.3Hz), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.37 (2H, br s), 8.35 (1H, t, J=5.5Hz)

Example 1 (32)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){3-(iso-propoxy)propylamino}methyleneamino]thiazole

m.p.: 119-120°C

IR (Nujol) : 3250, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 1.08 (6H, d, J=6.1Hz), 1.69 (2H, t, J=6.6Hz), 1.86 (3H, s), 3.21 (2H, q, J=6.6Hz), 3.3-3.5 (2H, m), 3.54 (1H, q, J=6.1Hz), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.36 (2H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{25}N_5O_3S$:

C 53.80; H 6.64; N 18.46

Found : C 54.04; H 6.85; N 18.27

Example 1 (33)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){3-(propoxy)propylamino}methyleneamino]thiazole

m.p.: 132-133°C

IR (Nujol) : 3300, 3100, 1660, 1595 cm^{-1}

NMR (DMSO-d_6, δ) : 0.86 (3H, t, J=7.3Hz), 1.42-1.79 (4H, m), 1.85 (3H, s), 3.17-3.46 (6H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.37 (2H, br s), 8.34 (1H, t, J=5.5Hz)

MASS (m/z) : 380 (M^++1)

Anal Calcd. for $C_{17}H_{25}N_5O_3S$:

C 53.81; H 6.64; N 18.46

Found : C 53.85; H 6.83; N 18.21

Example 1 (34)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-methoxyethoxy)ethylamino}methyleneamino]thiazole

m.p.: 134-137°C

IR (Nujol) : 3200, 3100, 1660, 1595 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.35 (5H, s), 3.48-3.59 (6H, m), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.59 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.40 (2H, br s), 8.35 (1H, t, J=5.5Hz)

MASS (m/z) : 382 (M^++1)

Example 1 (35)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(indol-2-yl)ethylamino}methyleneamino]thiazole

m.p. : 93-94°C

IR : 3150, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.94 (2H, t, J=7.1Hz), 3.45-3.55 (2H, m), 4.27 (2H, d,

J=5.5Hz), 6.26 (1H, d, J=3.2Hz), 6.44 (1H, d, J=3.2Hz), 6.79 (1H, s), 6.98 (1H, d, J=5.8Hz), 7.04 (1H, dd, J=1.5 and 3.6Hz), 7.10 (1H, d, J=5.8Hz), 7.19 (1H, d, J=1.5Hz), 7.35 (1H, d, J=7.5Hz), 7.43 (3H, br s), 7.63 (1H, d, J=7.5Hz), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{21}H_{22}N_6O_2S \cdot H_2O$:
C 57.25; H 5.49; N 19.08
Found : C 57.23; H 5.65; N 18.61

Example 1 (36)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-anilinoethylamino)methyleneamino]thiazole

m.p. : 113-115°C

IR (Nujol) : 3200, 1640, 1560 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.10-3.25 (2H, m), 3.32-3.45 (2H, m), 4.26 (2H, d, J=5.4Hz), 5.74 (1H, t, J=5.5Hz), 6.25 (1H, d, J=3.1Hz), 6.51-6.58 (2H, m), 6.65 (2H, d, J=7.7Hz), 6.80 (1H, s), 7.05-7.13 (2H, m), 7.49 (3H, br s), 8.34 (1H, t, J=5.4Hz)

Example 1 (37)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-methyl-2-butenylamino)methyleneamino]thiazole

m.p. : 166-168°C

IR (Nujol) : 3450, 1700, 1640, 1600, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.69 (6H, d, J=7.2Hz), 1.85 (3H, s), 3.73-3.78 (2H, m), 4.26 (2H, d, J=5.5Hz), 5.25 (1H, t, J=5.9Hz), 6.30 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.33 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{16}H_{21}N_5O_2S$:
C 55.31; H 6.09; N 20.16
Found : C 55.40; H 6.14; N 19.80

Example 1 (38)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(cyclopropylmethylamino)methyleneamino]thiazole

m.p. : 185-186°C

IR (Nujol) : 3400, 1660, 1640, 1590, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 0.20-0.25 (2H, m), 0.42-0.51 (2H, m), 0.98-1.10 (1H, m), 1.85 (3H, s), 3.02-3.09 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.31 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{15}H_{19}N_5O_2S$:

C 54.03; H 5.74; N 21.01

Found : C 54.19; H 5.70; N 20.67

Example 1 (39)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-methylpentylamino)methyleneamino]thiazole

m.p. : 193-194°C

IR (Nujol) : 3250, 1680, 1640, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (6H, d, J=6.6Hz), 1.19-1.27 (2H, m), 1.50-1.68 (3H, m), 1.86 (3H, s), 3.30-3.40 (2H, m), 4.29 (2H, d, J=5.5Hz), 6.37 (1H, d, J=3.2Hz), 6.82 (1H, d, J=3.2Hz), 7.33 (1H, s), 8.38 (1H, t, J=5.5Hz), 8.43 (3H, br s)

Example 1 (40)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-cyclohexylethylamino)methyleneamino]thiazole

m.p. : 129-130°C

IR (Nujol) : 3300, 1650, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 0.83-1.02 (2H, m), 1.08-1.30 (4H, m), 1.30-1.50 (4H, m), 1.56-1.84 (3H, m), 1.86 (3H, s), 3.16-3.24 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.57 (1H, d, J=3.2Hz), 6.83 (1H, s), 7.44 (3H, br s), 8.36

(1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{27}N_5O_2S$:

C 58.58; H 6.99; N 17.98

Found : C 58.26; H 7.21; N 18.03

Example 1 (41)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-cyclohexylpropylamino)methyleneamino]thiazole

m.p. : 220-221°C

IR (Nujol) : 3250, 1680, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88-0.94 (2H, m), 1.06-1.28 (2H, m), 1.56-1.71 (7H, m), 1.86 (3H, s), 3.27-3.40 (2H, m), 4.29 (2H, d, J=5.5Hz), 6.37 (1H, d, J=3.2Hz), 6.80 (1H, d, J=3.2Hz), 7.33 (1H, s), 8.38 (1H, t, J=5.5Hz), 8.41 (3H, br s)

Anal Calcd. for $C_{20}H_{29}N_5O_2S$:

C 59.52; H 7.24; N 17.36

Found : C 59.87; H 7.44; N 17.33

Example 1 (42)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-methoxyphenethylamino)methyleneamino]thiazole

m.p. : 125-128°C

IR (Nujol) : 3275, 1650, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.79 (2H, t, J=7.0Hz), 3.38-3.48 (2H, m), 3.73 (3H, s), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.77 (1H, s), 6.75-6.86 (3H, m), 7.18 (1H, t, J=8.0Hz), 7.40 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_3S$:

C 58.09; H 5.61; N 16.94

Found : C 58.41; H 5.58; N 16.59

Example 1 (43)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-cyclopentylethylamino)methyleneamino]thiazole

m.p. : 144-146°C

IR (Nujol) : 3450, 3300, 1650, 1590, 1540, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.02-1.22 (2H, m), 1.41-1.62 (6H, m), 1.64-1.98 (3H, m), 1.86 (3H, s), 3.13-3.26 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.32 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{18}H_{25}N_5O_2S$:

C 57.57; H 6.71; N 18.65

Found : C 57.95; H 6.76; N 18.52

Example 1 (44)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methylphenethylamino)methyleneamino]thiazole

m.p. : 175-176°C

IR (Nujol) : 3450, 3250, 1640, 1600, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.33 (3H, s), 2.81 (2H, t, J=8.0Hz), 3.16-3.35 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.53 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.09-7.22 (4H, m), 7.45 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_2S$:

C 60.43; H 5.83; N 17.62

Found : C 60.89; H 5.97; N 17.39

Example 1 (45)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2,4,6-trimethylphenethylamino)methyleneamino]thiazole

m.p. : 159-162°C

IR (Nujol) : 3400, 3250, 1650, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.18 (3H, s), 2.31 (6H, s), 2.73-2.82 (2H, m), 3.14-3.25 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz),

6.56 (1H, d, J=3.2Hz), 6.80 (3H, s), 7.50 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{22}H_{27}N_5O_2S$:

C 62.09; H 6.40; N 16.46

Found : C 62.30; H 6.51; N 16.31

Example 1 (46)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(benzylamino)methyleneamino]thiazole

m.p. : 189-191°C

IR (Nujol) : 3300, 1660, 1580, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.42 (2H, d, J=5.8Hz), 6.28 (1H, d, J=3.2Hz), 6.53 (1H, d, J=3.2Hz), 6.80 (1H, s), 7.23-7.40 (5H, m), 7.50 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{18}H_{19}N_5O_2S$:

C 58.52; H 5.18; N 18.96

Found : C 58.94; H 5.15; N 18.87

Example 1 (47)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methoxybenzylamino)methyleneamino]thiazole

m.p. : 159-160°C

IR (Nujol) : 3250, 1645, 1590, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.82 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.37 (2H, d, J=5.7Hz), 6.28 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.90-7.03 (2H, m), 7.24-7.31 (2H, m), 7.43 (3H, br s), 8.33 (1H, t, J=5.7Hz)

Anal Calcd. for $C_{19}H_{21}N_5O_3S$:

C 57.13; H 5.30; N 17.53

Found : C 57.37; H 5.37; N 17.38

Example 1 (48)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(5-methylfuran-2-yl)ethylamino}methyleneamino]thiazole

m.p. : 125-126°C

IR (Nujol) : 3250, 1655, 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.21 (3H, s), 2.78 (2H, t, J=6.9Hz), 3.37-3.47 (2H, m), 4.26 (2H, d, J=5.5Hz), 5.95 (1H, d, J=1.9Hz), 6.04 (1H, d, J=1.9Hz), 6.29 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.42 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{18}H_{21}N_5O_3S$:

C 55.80; H 5.46; N 18.08

Found : C 56.17; H 5.45; N 18.09

Example 1 (49)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-ethoxyphenethylamino)methyleneamino]thiazole

m.p. : 196-197°C

IR (Nujol) : 3450, 1625, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 1.36 (3H, t, J=6.9Hz), 1.85 (3H, s), 2.80 (2H, t, J=7.3Hz), 3.22-3.48 (2H, m), 4.04 (2H, q, J=6.9Hz), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.49 (1H, d, J=3.2Hz), 6.77 (1H, s), 6.82-6.97 (2H, m), 7.19 (2H, t, J=6.9Hz), 6.37 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{21}H_{25}N_5O_3S \cdot H_2O$:

C 56.61; H 6.11; N 15.72

Found : C 56.60; H 5.83; N 15.39

Example 1 (50)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-fluorophenethylamino)methyleneamino]thiazole

m.p. : 152-154°C

IR (Nujol) : 3450, 3275, 1655, 1580, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.85 (2H, t,

J=6.9Hz), 3.34-3.48 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.11-7.39 (4H, m), 7.44 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{20}FN_5O_2S$:

C 56.84; H 5.02; N 17.45

Found : C 57.09; H 5.14; N 17.34

Example 1 (51)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(cyclohexylidene)ethylamino}methyleneamino]thiazole

m.p. : 138-140°C

IR (Nujol) : 3250, 1650, 1580, 1515 cm^{-1}

NMR (DMSO-d, δ) : 1.24-1.55 (6H, m), 1.86 (3H, s), 2.01-2.19 (4H, m), 3.74-3.80 (2H, m), 4.27 (2H, d, J=5.5Hz), 5.20 (1H, t, J=6.9Hz), 6.29 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.31 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Example 1 (52)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(3-methylphenoxy)ethylamino}methyleneamino]thiazole

m.p. : 179-180°C

IR (Nujol) : 3450, 3300, 1650, 1595, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.28 (3H, s), 3.52-3.60 (2H, m), 3.88 (2H, t, J=5.8Hz), 4.26 (2H, d, J=5.5Hz), 6.55 (1H, d, J=3.1Hz), 6.56 (1H, d, J=3.1Hz), 6.75-6.81 (3H, m), 6.81 (1H, s), 7.13-7.21 (1H, m), 7.48 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_3S$:

C 58.09; H 5.61; N 16.94

Found : C 58.02; H 5.66; N 16.66

Example 1 (53)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-methylphenoxy)ethylamino}methyleneamino]thiazole

m.p. : 168-170°C

IR (Nujol) : 3300, 1650, 1590, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.17 (3H, s), 3.53-3.66 (2H m), 4.08 (2H, t, J=5.3Hz), 4.26 (2H, d, J=5.5Hz), 6.24 (1H, d, J=2.9Hz), 6.53 (1H, d, J=2.9Hz), 6.80 (1H, s), 6.87 (1H, d, J=7.3Hz), 6.99 (1H, d, J=7.9Hz), 7.14 (2H, d, J=7.3Hz), 7.50 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_3S$:

C 58.09; H 5.61; N 16.94

Found : C 58.14; H 5.64; N 16.72

Example 1 (54)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-chlorophenoxy)ethylamino}methyleneamino]thiazole

m.p. : 184-185°C

IR (Nujol) : 3300, 1660, 1600, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.55-3.66 (2H, m), 4.17 (2H, t, J=5.5Hz), 4.26 (2H, d, J=5.5Hz), 6.26 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.81 (1H, s), 6.93-7.01 (1H, m), 7.24-7.36 (2H, m), 7.41-7.46 (1H, m), 7.54 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Example 1 (55)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-methoxyphenoxy)ethylamino}methyleneamino]thiazole

m.p. : 170-171°C

IR (Nujol) : 3300, 1650, 1600, 1550, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.52-3.64 (2H, m), 3.75 (3H, s), 4.07 (2H, t, J=5.4Hz), 4.26 (2H, d, J=5.5Hz), 6.25 (2H, d, J=3.2Hz), 6.56 (2H, d, J=3.2Hz), 6.81 (1H, s), 6.84-7.08 (4H, m), 7.50

(3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_4S$:

C 55.93; H 5.40; N 16.31

Found : C 55.98; H 5.34; N 15.96

Example 1 (56)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-chlorophenethylamino)methyleneamino]thiazole

m.p. : 148-149°C

IR (Nujol) : 3300, 1660, 1580, 1515 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.45 (2H, t, J=6.9Hz), 3.39-3.45 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.22-7.46 (7H, m), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{20}ClN_5O_2S$:

C 54.61; H 4.82; N 16.76

Found : C 54.69; H 4.72; N 16.38

Example 1 (57)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-trifluoromethylphenethylamino)methyleneamino]thiazole

m.p. : 144-146°C

IR (Nujol) : 3400, 1650, 1600, 1525 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.01 (2H, t, J=7.1Hz), 3.40-3.51 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.81 (1H, s), 7.40-7.72 (7H, m), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{20}F_3N_5O_2S$:

C 53.21; H 4.47; N 15.51

Found : C 53.26; H 4.33; N 15.58

Example 1 (58)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-

methylbenzylamino)methyleneamino]thiazole

m.p. : 143-145°C

IR (Nujol) : 3300, 1660, 1630, 1585 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.32 (3H, s), 4.25 (2H, d, J=5.5Hz), 4.39 (2H, d, J=5.5Hz), 6.27 (1H, d, J=3.2Hz), 6.50 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.15-7.19 (3H, m), 7.24-7.33 (1H, m), 7.42 (3H, br s), 8.33 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{21}N_5O_2S$:

C 59.51; H 5.52; N 18.27

Found : C 59.86; H 5.86; N 18.17

Example 1 (59)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3,3-dimethylbutylamino)methyleneamino]thiazole

m.p. : 176-178°C

IR (Nujol) : 3300, 1660, 1640, 1600, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 0.92 (9H, s), 1.39-1.47 (2H, m), 1.85 (3H, s), 3.12-3.22 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.34 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{25}N_5O_2S$:

C 56.17; H 6.93; N 19.27

Found : C 56.52; H 6.84; N 19.03

Example 1 (60)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(1-naphthalenyl)ethylamino}methyleneamino]thiazole oxalate

m.p. : 219-220°C

IR (Nujol) : 3400, 3300, 1730, 1690, 1640, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.30-3.40 (2H, m), 3.54-3.67 (2H, m), 4.28 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 7.02 (1H, s), 7.39-7.64 (5H, m), 7.92-7.96 (2H, m),

8.33 (3H, br s), 8.37 (1H, t, J=5.5Hz)

Example 1 (61)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-isopropoxyethylamino)methyleneamino]thiazole

m.p. : 120-122°C

IR (Nujol) : 3300, 3100, 1660, 1590, 1550, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.11 (6H, d, J=6.1Hz), 1.85 (3H, s), 3.30-3.47 (2H, m), 3.45-3.50 (2H, m), 3.53-3.65 (1H, m), 4.26 (2H, d, J=5.5Hz), 6.36 (1H, d, J=3.2Hz), 6.60 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.38 (3H, br s), 8.36 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{16}H_{23}N_5O_3S$:

C 52.59; H 6.34; N 19.16

Found : C 52.24; H 6.19; N 18.89

Example 1 (62)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-ethoxybenzylamino)methyleneamino]thiazole

m.p. : 151-153°C

IR (Nujol) : 3300, 1650, 1590, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.35 (3H, t, J=6.9Hz), 1.85 (3H, s), 4.02 (2H, q, J=6.9Hz), 4.26 (2H, d, J=5.5Hz), 4.38 (2H, d, J=5.7Hz), 6.28 (1H, d, J=3.2Hz), 6.25 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.88-7.01 (2H, m), 7.21-7.28 (2H, m), 7.46 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_3S$:

C 58.10: H 5.61; N 16.94

Found : C 58.57; H 5.72; N 16.51

Example 1 (63)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(1-cyclohexenyl)ethylamino}methyleneamino]thiazole

m.p. : 168-169°C

IR (Nujol) : 3450, 1640, 1600, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.42-1.64 (4H, m), 1.85 (3H, s), 1.88-2.00 (4H, m), 2.13 (2H, t, J=7.0Hz), 3.21-3.30 (2H, m), 4.26 (2H, d, J=5.5Hz), 5.46 (1H, s), 6.30 (1H, d, J=3.2Hz), 6.57 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.39 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{25}N_5O_2S$:

C 58.89; H 6.50; N 18.07

Found : C 58.88; H 6.83; N 17.64

Example 1 (64)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(1-naphthalenylmethylamino)methyleneamino]thiazole

m.p. : 174-175°C

IR (Nujol) : 3250, 1640, 1580, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 4.25 (2H, d, J=5.4Hz), 4.87 (2H, d, J=5.4Hz), 6.24 (1H, d, J=3.2Hz), 6.45 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.45-7.63 (7H, m), 7.80-7.86 (1H, m), 7.90-7.99 (1H, m), 8.11-8.16 (1H, m), 8.34 (1H, t, J=5.4Hz)

Anal Calcd. for $C_{22}H_{21}N_5O_2S$:

C 62.99; H 5.05; N 16.69

Found : C 63.20; H 4.90; N 16.24

Example 1 (65)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-methyl-3-pentenylamino)methyleneamino]thiazole

m.p. : 124-126°C

IR (Nujol) : 3300, 1645, 1580, 1550, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.60 (3H, s), 1.67 (3H, s), 1.85 (3H, s), 2.15-2.22 (2H, m), 3.13-3.22 (2H, m), 4.26 (2H, d, J=5.5Hz), 5.15 (1H, t, J=6.9Hz),

6.30 (1H, d, J=3.2Hz), 6.58 (1H, d, J=3.2Hz), 6.83 (1H, s), 7.48 (3H, br s), 8.36 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{23}N_5O_2S$:

C 56.49; H 6.41; N 19.38

Found : C 56.31; H 6.55; N 19.02

Example 1 (66)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2,6-dimethylphenoxy)ethylamino}methyleneamino]thiazole oxalate

m.p. : 177-179°C

IR (Nujol) : 3200, 1700, 1630, 1580, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.24 (6H, d, J=3.1Hz), 3.55-3.66 (2H, m), 3.83-3.94 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.27 (1H, d, J=3.1Hz), 6.61 (1H, d, J=3.1Hz), 6.86 (1H, s), 6.90-7.05 (3H, m), 7.77 (3H, br s), 8.37 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{21}H_{25}N_5O_3S \cdot C_2H_2O_4$:

C 53.38; H 5.26; N 13.53

Found : C 53.68; H 5.61; N 13.52

Example 1 (67)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-ethoxy-3-butenylamino)methyleneamino]thiazole

m.p. : 128-129°C

IR (Nujol) : 3300, 1635, 1590, 1540, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.13 (3H, t, J=7.0Hz), 1.86 (3H, s), 3.14-3.60 (4H, m), 3.84-3.56 (1H, m), 4.27 (2H, d, J=5.5Hz), 5.23-5.34 (2H, m), 5.68-5.85 (1H, m), 6.30 (1H, d, J=3.2Hz), 6.60 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.36 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{23}N_5O_3S$:

C 54.09; H 6.14; N 18.56

Found : C 54.18; H 6.29; N 18.33

Example 1 (68)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-ethoxy-2-butenylamino)methyleneamino]thiazole

m.p. : 110-111°C

IR (Nujol) : 3450, 3300, 1650, 1590, 1550, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.10 (3H, t, J=7.0Hz), 1.86 (3H, s), 3.34-3.50 (2H, m), 3.80-3.87 (2H, m), 3.88-3.92 (2H, m), 4.27 (2H, d, J=5.5Hz), 5.70-5.73 (2H, m), 6.29 (1H, d, J=3.2Hz), 6.58 (1H, d, J=3.2Hz), 6.80 (1H, s), 7.42 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{23}N_5O_3S$:

C 54.09; H 6.14; N 18.56

Found : C 54.24; H 6.35; N 18.30

Example 1 (69)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(1,3-dioxolan-2-yl)ethylamino}methyleneamino]thiazole

m.p. : 151-152°C

IR (Nujol) : 3400, 3300, 1660, 1600, 1550, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.78-1.86 (2H, m), 1.86 (3H, s), 3.22-3.32 (2H, m), 3.74-3.83 (2H, m), 3.85-3.95 (2H, m), 4.27 (2H, d, J=5.5Hz), 4.88 (1H, t, J=4.7Hz), 6.30 (1H, d, J=3.2Hz), 6.58 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.42 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{16}H_{21}N_5O_4S$:

C 50.64; H 5.58; N 18.46

Found : C 50.73; H 5.61; N 18.05

Example 1 (70)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2,6-dimethylbenzylamino)methyleneamino]thiazole

m.p. : 134-136°C

IR (Nujol) : 3200, 1650, 1600, 1525 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.37 (6H, s), 4.25 (2H, d, J=5.5Hz), 4.38 (2H, d, J=5.5Hz), 6.23 (1H, d, J=3.1Hz), 6.38 (1H, d, J=3.1Hz), 6.79 (1H, s), 7.03-7.16 (3H, m), 7.29 (3H, br s), 8.32 (1H, t, J=5.5Hz)

Example (71)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2,3-dimethoxyphenethylamino)methyleneamino]thiazole

m.p. : 158-159°C

IR (Nujol) : 3300, 1650, 1620, 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.80 (2H, t, J=7.6Hz), 3.32-3.43 (2H, m), 3.75 (3H, s), 3.79 (3H, s), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.81-7.04 (3H, m), 7.40 (3H, br s), 8.33 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{21}H_{25}N_5O_4S$:

C 56.87; H 5.68; N 15.79

Found : C 57.32; H 5.69; N 15.63

Example 1 (72)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(1-ethylpropylamino)methyleneamino]thiazole oxalate

m.p. : 167-168°C

IR (Nujol) : 3250, 1720, 1620, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 0.90 (6H, t, J=7.2Hz), 1.43-1.66 (4H, m), 1.86 (3H, s), 3.51-3.68 (1H, m), 4.28 (2H, d, J=5.5Hz), 6.34 (1H, d, J=3.2Hz), 6.65 (1H, d, J=3.2Hz), 7.11 (1H, s), 8.36-8.40 (4H, m)

Anal Calcd. for $C_{16}H_{23}N_5O_2S \cdot C_2H_2O_4$:

C 49.19; H 5.73; N 15.94

Found : C 49.19; H 6.03; N 15.80

Example 1 (73)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-ethylbutylamino)methyleneamino]thiazole

m.p. : 109-111°C

IR (Nujol) : 3300, 1640, 1600, 1525 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (6H, t, J=7.0Hz), 1.28-1.40 (5H, m), 1.86 (3H, s), 3.11-3.16 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.53 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.20 (3H, br s), 8.33 (1H, t, J=5.5Hz)

Example 1 (74)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methylpentylamino)methyleneamino]thiazole

m.p. : 130-131°C

IR (Nujol) : 3300, 1660, 1640, 1590, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 0.82-0.91 (6H, m), 1.04-1.39 (4H, m), 1.50-1.70 (1H, m), 1.84 (3H, s), 2.93-3.18 (2H, m), 4.25 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.30 (3H, br s), 8.32 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{25}N_5O_2S \cdot 1/3H_2O$:
C 55.27; H 7.00; N 18.96

Found : C 55.24; H 7.10; N 18.93

Example 1 (75)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-methylthiazol-5-yl)ethylamino}methyleneamino]thiazole

m.p. : 145-147°C

IR (Nujol) : 3350, 1660, 1630, 1570 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.59 (3H, s), 3.00 (2H, t, J=6.6Hz), 3.37-3.47 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.2Hz), 6.80 (1H, s), 7.41 (1H, s), 7.48 (3H, br s), 8.36 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{20}N_6O_2S_2$:
C 50.47; H 4.98; N 20.78
Found : C 50.65; H 4.95; N 20.44

Example 1 (76)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){3-(pyridin-3-yl)propylamino}methyleneamino]thiazole

m.p. : 137-138°C

IR (Nujol) : 3200, 1600, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.75-1.86 (2H, m), 1.86 (3H, s), 2.67 (2H, t, J=7.3Hz), 3.14-3.24 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.57 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.28-7.35 (1H, m), 7.43 (3H, br s), 7.64-7.69 (1H, m), 8.35 (1H, t, J=5.5Hz), 8.40-8.47 (2H, m)

Anal Calcd. for $C_{19}H_{22}N_6O_2S$:
C 57.26; H 5.57; N 21.09
Found : C 57.61; H 5.70; N 20.94

Example 1 (77)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){3-(6-methylpyridin-2-yl)propylamino}methyleneamino]thiazole

m.p. : 140-145°C

IR (Nujol) : 3175, 1645, 1550 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 1.80-1.93 (2H, m), 2.43 (3H, s), 2.75 (2H, t, J=7.2Hz), 3.20-3.33 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.60 (1H, d, J=3.2Hz), 6.80 (1H, s), 7.07 (2H, d, J=7.6Hz), 7.46 (3H, br s), 7.59 (1H, t, J=7.6Hz), 8.36 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{24}N_6O_2S \cdot 3/4H_2O$:
C 56.39; H 6.03; N 19.73
Found : C 56.39; H 6.20; N 19.52

Example 1 (78)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2,4-dimethoxybenzylamino)methyleneamino]thiazole

m.p. : 156-157°C

IR (Nujol) : 3400, 1660, 1600, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.75 (3H, s), 3.81 (3H, s), 4.24-4.29 (4H, m), 6.28 (1H, d, J=3.2Hz), 6.48 (1H, d, J=2.3Hz), 6.53 (1H, d, J=2.3Hz), 6.58 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.19 (1H, d, J=3.2Hz), 7.36 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{20}H_{23}N_5O_4S$:

C 55.93; H 5.40; N 16.31

Found : C 55.82; H 5.35; N 16.08

Example 1 (79)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-nitrophenethylamino)methyleneamino]thiazole

m.p. : 133-134°C

IR (Nujol) : 3400, 1660, 1610, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.07 (2H, t, J=7.1Hz), 3.44-3.54 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.80 (1H, s), 7.44-7.56 (5H, m), 7.63-7.71 (1H, m), 7.96 (1H, d, J=8.1Hz), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{20}N_6O_4S$:

C 53.26; H 4.71; N 19.62

Found : C 53.67; H 4.80; N 19.61

Example 1 (80)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(tetrahydropyran-4-ylidene)ethylamino}methyleneamino]-thiazole

m.p. : 156-159°C

IR (Nujol) : 3300, 1640, 1600, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.02-2.32 (4H, m), 3.25-3.69 (4H, m), 3.77-3.98 (2H, m), 4.26 (2H, d, J=5.6Hz), 5.26-5.51 (1H, m), 6.30 (1H, d, J=3.2Hz), 6.57 (1H, d, J=3.2Hz), 6.78 (1H, s), 7.38 (3H, br s), 8.35 (1H, t, J=5.6Hz)

Anal Calcd. for $C_{18}H_{23}N_5O_3S$:
C 55.51; H 5.95; N 17.98
Found : C 55.73; H 6.25; N 17.59

Example 1 (81)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-piperidinobenzylamino)methyleneamino]thiazole oxalate

m.p. : 188-189°C

IR (Nujol) : 1610, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 1.47-1.60 (2H, m), 1.60-1.75 (4H, m), 1.85 (3H, s), 2.76-2.83 (4H, m), 4.26 (2H, d, J=5.5Hz), 4.44 (2H, d, J=5.0Hz), 6.29 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.81 (1H, s), 7.04-7.65 (4H, m), 7.66 (3H, br s), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{23}H_{28}N_6O_2S \cdot C_2H_2O_4$:
C 55.34; H 5.57; N 15.49
Found : C 55.02; H 5.77; N 15.09

Example 1 (82)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-n-propoxybenzylamino)methyleneamino]thiazole oxalate

m.p. : 153-154°C

NMR (DMSO-d_6, δ) : 1.00 (3H, t, J=7.4Hz), 1.71-1.83 (2H, m), 1.85 (3H, s), 3.98 (2H, t, J=6.4Hz), 4.26 (2H, d, J=5.5Hz), 4.39 (2H, d, J=4.7Hz), 6.28 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.87-7.06 (2H, m), 7.20-7.38 (2H, m), 7.52 (3H, br s), 8.37 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{21}H_{25}N_5O_3S \cdot C_2H_2O_4$:

C 53.38; H 5.26; N 13.53
Found : C 53.22; H 5.11; N 13.71

Example 1 (83)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-piperidinoethylamino)methyleneamino]thiazole oxalate

m.p. : 125-128°C

IR (Nujol) : 3250, 1680, 1620, 1580, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.45-1.58 (2H, m), 1.64-1.82 (4H, m), 1.86 (3H, s), 3.01-3.18 (6H, m), 3.52-3.62 (2H, m), 4.28 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.65 (1H, d, J=3.2Hz), 6.87 (1H, s), 7.94 (3H, br s), 8.41 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{18}H_{26}N_6O_2S \cdot C_2H_2O_4$:
C 49.99; H 5.87; N 17.49
Found : C 50.36; H 5.86; N 17.32

Example 1 (84)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-isopropoxybenzylamino)methyleneamino]thiazole oxalate

m.p. : 155-156°C

IR (Nujol) : 3150, 1700, 1615 cm^{-1}

NMR (DMSO-d_6, δ) : 1.30 (6H, t, J=2.5Hz), 4.26 (2H, d, J=5.5Hz), 4.36 (2H, d, J=5.1Hz), 4.58-4.72 (1H, m), 6.28 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.78 (1H, s), 6.86-7.08 (2H, m), 7.19-7.38 (2H, m), 7.54 (3H, br s), 8.37 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{21}H_{25}N_5O_3S \cdot C_2H_2O_4$:
C 53.38; H 5.26; N 13.53
Found : C 53.51; H 4.89; N 13.41

Example 1 (85)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-hydroxybenzylamino)methyleneamino]thiazole

m.p. : 213-214°C

IR (Nujol) : 3350, 1700, 1640, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 4.27 (4H, d, J=5.5Hz), 6.31 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.73-6.85 (3H, m), 7.06-7.16 (5H, m), 8.34 (1H, t, J=5.5Hz), 10.01 (1H, br s)

Anal Calcd. for $C_{18}H_{19}N_5O_3S$:

C 56.09; H 4.97; N 18.17

Found : C 56.05; H 5.08; N 18.56

Example 1 (86)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(cyclopentylmethylamino)methyleneamino]thiazole

m.p. : 168-169°C

IR (Nujol) : 3250, 1665, 1600, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 1.13-1.32 (2H, m), 1.48-1.60 (4H, m), 1.65-1.82 (2H, m), 1.85 (3H, s), 2.00-2.14 (1H, m), 3.08-3.14 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.54 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.27 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{17}H_{23}N_5O_2S$:

C 56.49; H 6.41; N 19.38

Found : C 56.32; H 6.61; N 19.00

Example 1 (87)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-methoxybenzylamino)methyleneamino]thiazole oxalate

m.p. : 178-179°C

IR (Nujol) : 3150, 1580, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.74 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.38 (2H, d, J=5.7Hz), 6.28 (1H, d, J=3.1Hz), 6.53 (1H, d, J=3.1Hz), 6.80 (1H, s), 6.85-7.07 (3H, m), 7.22-7.37 (1H, m), 7.53 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{21}N_5O_3S \cdot C_2H_2O_4$:
C 51.53; H 4.74; N 14.31
Found : C 51.94; H 4.66; N 14.31

Example 1-(88)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-methoxybenzylamino)methyleneamino]thiazole

m.p. : 154-156°C

IR (Nujol) : 3250, 1650, 1590, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.73 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.33 (2H, d, J=5.6Hz), 6.28 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.79 (1H, s), 6.91 (2H, d, J=8.6Hz), 7.27 (2H, d, J=8.6Hz), 7.46 (3H, br s), 8.35 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{21}N_5O_3S \cdot 1/2H_2O$:
C 55.86; H 5.43; N 17.15
Found : C 56.03; H 5.38; N 16.93

Example 1 (89)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-trifluoromethylanilino)methyleneamino]thiazole

m.p. : 180-182°C

IR (Nujol) : 3300, 1640, 1520 cm^{-1}

NM R (DMSO-d_6, δ) : 1.87 (3H, s), 4.29 (2H, d, J=5.5Hz), 6.33 (1H, d, J=3.0Hz), 6.71 (1H, d, J=3.0Hz), 7.03 (1H, s), 7.63-7.77 (4H, m), 7.92 (2H, br s), 8.37 (1H, t, J=5.5Hz), 9.20 (1H, s)

Anal Calcd. for $C_{18}H_{16}F_3N_5O_2S \cdot 1/2H_2O$:
C 50.00; H 3.96; N 16.20
Found : C 49.80; H 3.75; N 16.24

Example 1 (90)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(3-chloroanilino)methyleneamino]thiazole

m.p. : 195-197°C

IR (Nujol) : 3400, 1640, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 4.28 (2H, d, J=5.5Hz), 6.33 (1H, d, J=3.2Hz), 6.69 (1H, d, J=3.2Hz), 7.00 (1H, s), 7.01-7.05 (1H, m), 7.27-7.35 (2H, m), 7.77 (1H, s), 7.86 (2H, br s), 8.36 (1H, t, J=5.5Hz), 9.01 (1H, s)

Anal Calcd. for $C_{17}H_{16}ClN_5O_2S \cdot 1/3H_2O$:
C 51.59; H 4.24; N 17.69
Found : C 51.64; H 4.44; N 17.33

Example 1 (91)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-fluoroanilino)methyleneamino]thiazole

m.p. : 158-159°C

IR (Nujol) : 3350, 1630, 1515 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 4.28 (2H, d, J=5.5Hz), 6.32 (1H, d, J=3.2Hz), 6.66 (1H, d, J=3.2Hz), 6.95 (1H, s), 7.15 (2H, t, J=8.8Hz), 7.47-7.54 (2H, m), 7.76 (2H, br s), 8.36 (1H, t, J=5.5Hz), 8.87 (1H, br s)

Anal Calcd. for $C_{17}H_{16}FN_5O_2S$:
C 54.68; H 4.32; N 18.76
Found : C 54.22; H 4.26; N 18.59

Example 1 (92)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(m-anisidino)methyleneamino]thiazole

m.p. : 173-175°C

IR (Nujol) : 3300, 1630, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.75 (3H, s), 4.28 (2H, d, J=5.5Hz), 6.32 (1H, d, J=3.2Hz), 6.56-6.61 (1H, m), 6.67 (1H, d, J=3.2Hz), 6.96 (1H, s), 6.95-6.99 (1H, m), 7.20 (1H, t, J=8.1Hz), 7.27 (1H, s), 7.78 (2H, br s), 8.36 (1H, t, J=5.5Hz), 8.89 (1H, br s)

Anal Calcd. for $C_{18}H_{19}N_5O_3S$:
C 56.09; H 4.97; N 18.17
Found : C 55.78; H 5.05; N 17.94

Example 1 (93)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(o-anisidino)methyleneamino]thiazole

m.p. : 132-133°C

IR (Nujol) : 3350, 1660, 1620, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.87 (3H, s), 4.28 (2H, d, J=5.5Hz), 6.32 (1H, d, J=3.2Hz), 6.69 (1H, d, J=3.2Hz), 6.91 (1H, s), 6.88-7.03 (3H, m), 7.95 (2H, br s), 8.10 (1H, d, J=7.3Hz), 8.36 (1H, t, J=5.5Hz), 8.44 (1H, br s)

Anal Calcd. for $C_{18}H_{19}N_5O_3S$:
C 56.09; H 4.97; N 18.17
Found : C 55.72; H 5.04; N 18.10

Example 1 (94)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(p-anisidino)methyleneamino]thiazole

m.p. : 144-146°C

IR (Nujol) : 3300, 1620, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 3.73 (3H, s), 4.27 (2H, d, J=5.5Hz), 6.31 (1H, d, J=3.2Hz), 6.62 (1H, d, J=3.2Hz), 6.90 (1H, s), 6.91 (2H, d, J=8.9Hz), 7.35 (2H, d, J=8.9Hz), 7.66 (2H, br s), 8.38 (1H, t, J=5.5Hz), 8.77 (1H, br s)

Anal Calcd. for $C_{18}H_{19}N_5O_3S$:
C 56.09; H 4.97; N 18.17
Found : C 55.66; H 4.81; N 17.95

Example 1 (95)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-phenoxymethylbenzylamino)methyleneamino]thiazole oxalate

m.p. : 195-196°C
IR (Nujol) : 3100, 1710, 1670, 1630 cm^{-1}
NMR (DMSO-d_6, δ) : 1.83 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.57 (2H, d, J=5.0Hz), 5.22 (2H, s), 6.28 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.88-7.56 (10H, m), 7.93 (2H, br s), 8.34 (1H, t, J=5.5Hz)
MASS (m/z) : 476 (M^++1) free of compound
Anal Calcd. for $C_{27}H_{29}N_5O_7S$:
C 57.63; H 5.15; N 12.34
Found : C 57.80; H 4.92; N 12.48

Example 1 (96)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){(4-ethyl-6-methyl)-2,4-heptadienylamino}methyleneamino]thiazole

m.p. : 177-179°C
IR (Nujol) : 3300, 3200, 1660, 1630, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 0.88-1.10 (9H, m), 1.86 (3H, s), 2.22 (2H, q, J=7.6Hz), 2.55-2.75 (1H, m), 4.03-4.15 (2H, m), 4.29 (2H, d, J=5.6Hz), 5.27 (1H, d, J=9.7Hz), 5.62-5.78 (1H, m), 6.18 (1H, d, J=15.9Hz), 6.35 (1H, d, J=3.3Hz), 6.81 (1H, d, J=3.3Hz), 7.34 (1H, s), 8.38 (1H, t, J=5.6Hz)

Example 1 (97)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(piperidinomethyl)benzylamino}methyleneamino]thiazole dihydrochloride

m.p. : 190-195°C
IR (Nujol) : 3300, 1670, 1630, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 1.51-2.03 (6H, m), 1.86 (3H, s), 2.96-3.50 (4H, m), 4.27 (2H, d, J=5.5Hz), 4.39 (2H, br s), 5.08 (2H, d, J=5.2Hz), 6.33 (1H, d, J=3.2Hz), 6.81 (1H, d, J=3.2Hz), 7.33 (1H, s),

7.39-7.59 (3H, m), 7.73 (1H, d, J=6.8Hz), 8.41 (1H, t, J=5.5Hz), 8.96 (2H, br s), 9.44 (1H, br s)

MASS (m/z) : 467 (M^++1) free of compound

Anal Calcd. for $C_{24}H_{32}N_6O_2SCl_2$:

C 49.43; H 6.36; N 14.42

Found : C 49.45; H 6.45; N 14.27

Example 1 (98)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(N,N-dimethylsulfamoyl)benzylamino}methyleneamino]thiazole oxalate

m.p. : 161-163°C

IR (Nujol) : 3260, 1760, 1700, 1645, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.78 (6H, s), 4.26 (2H, d, J=5.5Hz), 4.81 (2H, d, J=4.4Hz), 6.30 (1H, d, J=3.3Hz), 6.62 (1H, d, J=3.3Hz), 6.93 (1H, s), 7.51-7.89 (4H, m), 8.35 (1H, t, J=5.5Hz)

MASS (m/z) : 477 (M^++1) free of compound

Anal Calcd. for $C_{20}H_{24}N_6O_4S_2 \cdot 1.5H_2O$:

C 44.51; H 4.92; N 14.16

Found : C 44.55; H 5.16; N 13.37

Example 1 (99)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(8-quinolylmethylamino)methyleneamino]thiazole

m.p. : 206-207°C

IR (Nujol) : 3270, 1645, 1590, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 4.12 (2H, d, J=5.2Hz), 5.02 (2H, d, J=5.8Hz), 6.28 (1H, d, J=3.2Hz), 6.47 (1H, d, J=3.2Hz), 6.77 (1H, s), 7.50-7.96 (5H, m), 8.35 (1H, t, J=5.8Hz), 8.42 (1H, dd, J=1.7 and 8.3Hz), 8.99 (1H, dd, J=1.7 and 4.2Hz)

MASS (m/z) : 421 (M^++1)

Anal Calcd. for $C_{21}H_{20}N_6O_2S$: C 59.99; H 4.79; N 19.99

Found : C 59.97; H 4.92; N 19.66

Example 1 (100)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino){2-(2-methoxyethoxy)benzylamino}methyleneamino]thiazole oxalate

m.p. : 183-184°C

IR (Nujol) : 3370, 1730, 1700, 1630, 1550 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 3.30 (3H, s), 3.67 (2H, t, J=4.5Hz), 4.14 (2H, t, J=4.5Hz), 4.26 (2H, d, J=5.5Hz), 4.47 (2H, d, J=5.0Hz), 6.29 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.92-7.08 (3H, m), 7.26-7.33 (2H, m), 8.34 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{23}H_{27}N_5O_8S$:

C 51.68; H 5.28; N 13.10

Found : C 51.65; H 5.04; N 12.98

Example 1 (101)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(n-pentylamino)methyleneamino]thiazole

m.p. : 133-134°C

IR (Nujol) : 3300, 3100, 1650, 1590, 1550, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (3H, t, J=6.6Hz), 1.22-1.61 (6H, m), 1.86 (3H, s), 3.10-3.23 (2H, m), 4.27 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.32 (2H, br s), 8.35 (1H, t, J=5.5Hz)

Example 2 (1)

A solution of 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(2-hydroxybenzylamino)methyleneamino]thiazole (772 mg), 2-iododimethylacetamide (1.6 g) and potassium

carbonate (1.1 g) in dimethylformamide (5 ml) was stirred for 6 hours at room temperature. The mixture was diluted with water (50 ml) and extracted with ethyl acetate (30 ml). The extract was washed with brine, dried over anhydrous magnesium sulfate, and then evaporated in vacuo. The residue was purified by column chromatography on silica gel eluting with (3% methanol/chloroform) to give 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino){2-(N,N-dimethylcarbamoylmethoxy)benzylamino}methyleneamino]-thiazole (0.26 g).

m.p. : 198-199°C

IR (Nujol) : 3370, 3230, 1660, 1650, 1620, 1550 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.85 (3H, s), 3.01 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.44 (2H, d, J=5.7Hz), 4.90 (2H, s), 6.28 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.79 (1H, s), 6.90-7.29 (4H, m), 7.49 (2H, br s), 8.35 (1H, t, J=5.7Hz)

Anal Calcd. for $C_{21}H_{26}N_6O_4S \cdot 1/3H_2O$:

C 55.43; H 5.64; N 17.63

Found : C 55.44; H 5.50; N 17.45

The following compound was obtained according to a similar manner to that of Example 2 (1).

Example 2 (2)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-ethoxycarbonylmethoxybenzylamino)methyleneamino]thiazole

m.p. : 133-135°C

IR (Nujol) : 3350, 1740, 1650, 1630, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.21 (3H, t, J=7.1Hz), 1.85 (3H, s), 4.17 (2H, q, J=7.1Hz), 4.25 (2H, d, J=5.5Hz), 4.44 (2H, d, J=5.8Hz), 4.85 (2H, s), 6.28 (1H, d, J=3.2Hz), 6.52 (1H, d, J=3.2Hz), 6.79 (1H, s), 6.79-7.00 (2H, m), 7.18-7.31 (2H, m), 7.50 (1H, br s), 8.34 (1H, t, J=5.8Hz)

Anal Calcd. for $C_{22}H_{25}N_5O_5S$:
C 56.04; H 5.34; N 14.85
Found : C 55.93; H 5.47; N 14.58

Example 3 (1)

A solution of 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(2-nitrophenethylamino)methyleneamino]thiazole (3.3 g) in methanol was hydrogenated over 10% palladium on carbon at room temperature. The catalyst was removed by filtration and the solvent was evaporated in vacuo. The residue was dissolved in ethyl acetate. The solution was washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was recrystallized from a mixture of ethyl acetate and diethyl ether to give 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(2-aminophenethylamino)methyleneamino]thiazole (2.24 g).

m.p. : 161-162°C

IR (Nujol) : 3350, 1650, 1610, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.63-2.71 (2H, m), 3.20-3.40 (2H, m), 4.27 (2H, d, J=5.5Hz), 5.18 (2H, br s), 6.30 (1H, d, J=3.2Hz), 6.48 (1H, t, J=7.3Hz), 6.59 (1H, d, J=3.2Hz), 6.60-6.71 (1H, m), 6.83 (1H, s), 6.88-6.96 (2H, m), 7.53 (3H, br s), 8.38 (1H, t, J=5.5Hz)

Anal Calcd. for $C_{19}H_{22}N_6O_2S$:
C 56.11; H 5.61; N 18.70
Found : C 56.19; H 5.36; N 18.68

Example 3 (2)

To a solution of 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(2-aminophenethylamino)methyleneamino]thiazole (2.0 g) and triethylamine (0.7 ml) in dichloromethane (40 ml) and N,N-dimethylformamide (13 ml) was added dropwise acetic anhydride (0.7 ml), and the mixture was stirred for 1 hour at room temperature. The resulting precipitate was

collected by filtration and recrystallized from mixture of methanol and ethyl acetate to give 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(2-acetylaminophenethylamino}-methyleneamino]thiazole (1.25 g).

m.p. : 224-225°C

IR (Nujol) : 3250, 1625, 1590, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 2.06 (3H, s), 2.73-2.89 (2H, m), 3.33-3.42 (2H, m), 4.26 (2H, d, J=5.5Hz), 6.29 (1H, d, J=3.2Hz), 6.55 (1H, d, J=3.2Hz), 6.79 (1H, s), 7.14-7.40 (7H, m), 8.35 (1H, t, J=5.5Hz), 9.37 (1H, s)

Anal Calcd. for $C_{21}H_{24}N_6O_3S \cdot 1/2H_2O$:
C 56.11; H 5.61; N 18.70

Found : C 56.19; H 5.36; N 18.68

Example 4 (1)

A solution of 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(cyclohexylmethylamino)methyleneamino]thiazole (4.0 g) and concentrated hydrochloric acid (8 ml) in ethanol (80 ml) was refluxed for 26 hours. The reaction mixture was concentrated in vacuo to a half volume, and the resulting precipitate was collected by filtration to give 4-(5-aminomethylfuran-2-yl)-2-[(amino)-(cyclohexylmethylamino)methyleneamino]thiazole dihydrochloride (2.72 g).

IR (Nujol) : 3100, 2600, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.97-1.38 (6H, m), 1.45-1.81 (5H, m), 3.28 (2H, t, J=6.0Hz), 4.12 (2H, s), 6.69 (1H, d, J=3.3Hz), 6.88 (1H, d, J=3.3Hz), 7.41 (1H, s), 8.63 (5H, br s), 9.18 (1H, br s), 12.90 (1H, br s)

The following compounds were obtained according to a similar manner to that of Example 4 (1).

Example 4 (2)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-methylpropylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.98 (6H, d, J=6.7Hz), 1.80-2.00 (1H, m), 3.27 (2H, t, J=6.2Hz), 4.13 (2H, s), 6.69 (1H, d, J=3.2Hz), 6.90 (1H, d, J=3.2Hz), 7.42 (1H, s), 8.65 (5H, br s), 9.20 (1H, br s), 12.90 (1H, br s)

Example 4 (3)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(3-methylbutylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3200, 3100, 2650, 1700, 1640, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 0.93 (6H, d, J=6.5Hz), 1.50 (2H, q, J=7.0Hz), 1.64-1.78 (1H, m), 3.3-3.5 (2H, m), 4.13 (2H, br s), 6.69 (1H, d, J=3.2Hz), 6.90 (1H, d, J=3.2Hz), 7.42 (1H, s), 8.68 (5H, br s), 9.04 (1H, br s)

Example 4 (4)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-methylbutylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.90 (3H, t, J=7.7Hz), 0.97 (3H, d, J=6.7Hz), 1.15-1.29 (1H, m), 1.41-1.70 (2H, m), 3.30-3.50 (2H, m), 4.13 (2H, br s), 6.69 (1H, d, J=3.2Hz), 6.89 (1H, d, J=3.2Hz), 7.43 (1H, s), 8.71 (5H, br s), 9.16 (1H, br s), 13.0 (1H, br s)

Example 4 (5)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2,2-dimethylpropylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 1.00 (9H, s), 3.31 (2H, d, J=5.7Hz), 4.08-4.16 (2H, m), 6.70 (1H, d, J=3.2Hz), 6.86 (1H, d, J=3.2Hz), 7.45 (1H, s), 8.70 (5H, br s), 9.33 (1H, br s), 13.10 (1H, br s)

Example 4 (6)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(n-heptylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3450, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.86 (3H, t, J=6.7Hz), 1.20-1.50 (8H, m), 1.50-1.65 (2H, m), 3.18-3.49 (2H, m), 4.15 (2H, br s), 6.67 (1H, d, J=3.2Hz), 6.91 (1H, d, J=3.2Hz), 8.2-8.6 (5H, br s), 8.90 (1H, br s)

Example 4 (7)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(n-octylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.85 (3H, t, J=6.7Hz), 1.25 (10H, br s), 1.50-1.70 (2H, m), 3.20-3.50 (2H, m), 4.14 (2H, br s), 6.67 (1H, d, J=3.2Hz), 6.91 (1H, d, J=3.2Hz), 7.40 (1H, s), 8.61 (5H, br s), 9.00 (1H, br s), 12.70 (1H, br s)

Example 4 (8)

4-(5-Aminomethylfuran-2-yl)-2-[(amino){2-(2-methylthiazol-5-yl)ethylamino}methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1670, 1610, 1490 cm^{-1}

NMR (DMSO-d_6, δ) : 2.67 (3H, s), 3.16 (2H, t, J=6.8Hz), 3.70-3.80 (2H, m), 4.13 (2H, d, J=5.4Hz), 6.68 (1H, d, J=3.2Hz), 6.88 (1H, d,

J=3.2Hz), 7.42 (1H, s), 7.71 (1H, s), 8.68 (3H, br s), 8.81 (2H, br s), 9.14 (1H, br s), 12.90 (1H, br s)

Example 4 (9)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-n-propoxybenzylamino)methyleneamino]thiazole dihydrochloride

IR (Neat) : 3300, 1730, 1660, 1590, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 1.00 (3H, t, J=7.4Hz), 1.66-1.85 (2H, m), 3.89-4.08 (4H, m), 4.38 (2H, t, J=7.6Hz), 6.23 (1H, d, J=3.2Hz), 6.48 (1H, d, J=3.2Hz), 6.76 (1H, s), 6.88-7.01 (2H, m), 7.09-7.31 (2H, m), 7.44 (5H, m)

Example 4 (10)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(3-phenylpropylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1700, 1640, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.84-1.95 (2H, m), 2.72 (2H, t, J=7.2Hz), 3.39-3.50 (2H, m), 4.12 (2H, d, J=5.5Hz), 6.68 (1H, d, J=3.2Hz), 6.96 (1H, d, J=3.2Hz), 7.15-7.33 (5H, m), 7.43 (1H, s), 8.72 (5H, br s), 9.14 (1H, br s), 12.89 (1H, br s)

Example 4 (11)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-phenethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1700, 1640, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 2.94 (3H, t, J=6.9Hz), 3.64-3.78 (2H, m), 4.14 (2H, br s), 6.66 (1H, d, J=3.2Hz), 6.78 (1H, d, J=3.2Hz), 7.22-7.37 (6H, m), 8.60 (5H, br s), 9.00-9.20 (1H, br s), 12.60-12.80 (1H, br s)

Example 4 (12)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(4-methyl-n-pentylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3300, 1700, 1640, 1505 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (6H, d, J=6.6Hz), 1.20-1.31 (2H, m), 1.51-1.64 (3H, m), 3.36-3.46 (2H, m), 4.13 (2H, br s), 6.69 (1H, d, J=3.2Hz), 6.94 (1H, d, J=3.2Hz), 7.42 (1H, s), 8.70 (5H, br s), 9.04 (1H, br s)

Example 4 (13)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(cyclopropylmethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3300, 1700, 1640, 1505 cm^{-1}

NMR (DMSO-d_6, δ) : 0.31-0.38 (2H, m), 0.52-0.61 (2H, m), 1.10-1.28 (2H, m), 3.30-3.37 (2H, m), 4.14 (2H, s), 6.69 (1H, d, J=3.4Hz), 6.92 (1H, d, J=3.4Hz), 7.42 (1H, s), 8.68 (5H, br s), 9.21 (1H, br s), 12.92 (1H, br s)

Example 4 (14)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(3,3-dimethylbutylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1695, 1640, 1550, 1525 cm^{-1}

NMR (DMSO-d_6, δ) : 0.95 (9H, s), 1.57-1.59 (2H, m), 3.39-3.42 (2H, m), 4.14 (2H, br s), 6.69 (1H, d, J=3.3Hz), 6.92 (1H, d, J=3.3Hz), 7.42 (1H, s), 8.68 (5H, br s), 8.96 (1H, br s), 12.90 (1H, br s)

Example 4 (15)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-cyclohexylethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1700, 1640, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 0.89-1.80 (13H, m), 3.30-3.44 (2H, m), 4.15 (2H, s), 6.68 (1H, d, J=3.2Hz), 6.91 (1H, d, J=3.2Hz), 7.40 (1H, s), 8.61 (5H, br s), 9.06 (1H, br s), 12.80 (1H, br s)

Example 4 (16)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-methoxyphenethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1690, 1640, 1515 cm^{-1}

NMR (DMSO-d_6, δ) : 2.91 (2H, t, J=6.8Hz), 3.61-3.70 (2H, m), 3.76 (3H, s), 4.12 (2H, br s), 6.66 (1H, d, J=3.2Hz), 6.74 (1H, d, J=3.2Hz), 6.83-6.98 (2H, m), 7.17-7.29 (2H, m), 7.40 (1H, s), 8.67 (5H, br s), 9.07 (1H, br s), 12.91 (1H, br s)

Example 4 (17)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-methylphenethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1690, 1640, 1520 cm^{-1}

NMR (DMSO-d_6, δ): 2.32 (3H, s), 2.93 (2H, t, J=7.1Hz), 3.60-3.72 (2H, m), 4.13 (2H, br s), 6.66 (1H, d, J=3.3Hz), 6.78 (1H, d, J=3.3Hz), 7.10-7.21 (3H, m), 7.26-7.31 (1H, m), 7.39 (1H, s), 8.65 (5H, br s), 9.13 (1H, br s), 12.95 (1H, br s)

Example 4 (18)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(2-phenylbenzylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3100, 1670, 1610, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 4.10 (2H, d, J=5.3Hz), 4.61 (2H,

d, J=4.7Hz), 6.64 (1H, d, J=2.7Hz), 7.28-7.57 (11H, m), 8.74 (5H, br s), 9.33 (1H, br s), 13.02 (1H, br s)

Example 4 (19)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(8-quinolylmethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3150, 1625 cm^{-1}

NMR (DMSO-d_6, δ) : 4.12 (2H, d, J=5.3Hz), 5.33 (2H, d, J=5.5Hz), 5.65 (2H, br s), 6.67 (1H, d, J=3.3Hz), 6.74 (1H, d, J=3.3Hz), 7.41 (1H, s), 7.69-7.80 (2H, m), 8.03-8.14 (2H, m), 8.64-8.83 (4H, m), 8.97 (1H, br s), 9.05-9.08 (1H, m), 9.70 (1H, br s)

Example 4 (20)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(1-naphthalenylmethylamino)methyleneamino]thiazole dihydrochloride

IR (Nujol) : 3250, 1680, 1640, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 4.08 (2H, br s), 5.21 (2H, d, J=5.2Hz), 6.42 (1H, d, J=3.2Hz), 6.59 (1H, d, J=3.2Hz), 7.38 (1H, s), 7.50-7.68 (4H, m), 7.95-8.05 (2H, m), 8.15-8.19 (1H, m), 8.69 (3H, br s), 8.86 (2H, br s), 9.64 (1H, br s), 13.10 (1H, br s)

Example 4 (21)

4-(5-Aminomethylfuran-2-yl)-2-[(amino)(n-pentylamino)methyleneamino]thiazole dihydrochloride

m.p. : 275-279°C

IR (Nujol) : 3450, 3300, 1700, 1660, 1630, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (3H, t, J=7.0Hz), 1.25-1.72

(6H, m), 3.39 (2H, br s), 4.13 (2H, br s), 6.69 (1H, d, J=3.3Hz), 6.93 (1H, d, J=3.3Hz), 7.42 (1H, s), 8.69 (5H, br s)

Example 5 (1)

A solution of 4-(5-aminomethylfuran-2-yl)-2-[(amino)(cyclohexylmethylamino)methyleneamino]thiazole dihydrochloride (2.7 g) and potassium cyanate (1.13 g) in water (55 ml) was stirred at room temperature for 5 hours. The resulting precipitate was collected by filtration and recrystallized from a mixture of methanol and toluene to give 4-(5-ureidomethylfuran-2-yl)-2-[(amino)(cyclohexylmethylamino)methyleneamino]thiazole (1.52 g).

m.p.: 166-167°C

IR (Nujol) : 3250, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 0.93-1.39 (6H, m), 1.40-1.80 (5H, m), 3.07 (2H, t, J=6.1Hz), 4.19 (2H, d, J=5.6Hz), 5.58 (2H, s), 6.27 (1H, d, J=3.2Hz), 6.41 (1H, t, J=5.6Hz), 6.57 (1H, d, J=3.2Hz), 6.87 (1H, s), 7.48 (3H, br s)

Anal Calcd. For $C_{17}H_{24}N_6O_2S \cdot H_2O$:
C 51.76; H 6.64; N 21.30
Found : C 51.52; H 6.51; N 21.11

The following compounds were obtained according to a similar manner to that of Example 5 (1).

Example 5 (2)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-methylpropylamino)methyleneamino]thiazole

m.p.: 209-211°C

IR (Nujol) : 3350, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.96 (6H, d, J=6.6Hz), 1.8-1.9 (1H, m), 3.18 (2H, t, J=6.0Hz), 4.21 (2H, d,

J=5.6Hz), 5.62 (2H, s), 6.31 (1H, d, J=3.4Hz), 6.47 (1H, t, J=5.6Hz), 6.73 (1H, d, J=3.4Hz), 7.18 (1H, s), 8.22 (3H, br s)

Example 5 (3)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(3-methylbutylamino)methyleneamino]thiazole

m.p.: 159-161°C

IR (Nujol) : 3250, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 0.91 (6H, d, J=6.5Hz), 1.43 (2H, q, J=7.0Hz), 1.6-1.7 (1H, m), 3.20-3.40 (2H, m), 4.20 (2H, d, J=5.5Hz), 5.59 (2H, s), 6.28 (1H, d, J=3.2Hz), 6.42 (1H, t, J=5.5Hz), 6.62 (1H, d, J=3.2Hz), 6.93 (1H, s), 7.70 (3H, br s)

Anal Calcd. for $C_{15}H_{22}N_6O_2S \cdot H_2O$:

C 48.90; H 6.57; N 22.81

Found : C 48.83; H 6.24; N 22.48

Example 5 (4)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-methylbutylamino)methyleneamino]thiazole

m.p.: 144-145°C

IR (Nujol) : 3250, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 0.85-0.93 (6H, m), 1.10-1.24 (1H, m), 1.37-1.62 (2H, m), 3.0-3.18 (2H, m), 4.19 (2H, d, J=5.7Hz), 5.58 (2H, s), 6.27 (1H, d, J=3.2Hz), 6.41 (1H, t, J=5.7Hz), 6.56 (1H, d, J=3.2Hz), 6.84 (1H, s), 7.44 (3H, br s)

Anal Calcd. for $C_{15}H_{22}N_6O_2S$:

C 51.41; H 6.33; N 23.98

Found : C 51.75; H 6.24; N 23.82

Example 5 (5)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2,2-dimethylpropylamino)methyleneamino]thiazole oxalate

m.p.: 234-235°C

IR (Nujol) : 3400, 3200, 1700, 1650 cm^{-1}

NMR (DMSO-d_6, δ) : 0.96 (9H, s), 3.11 (2H, d, J=5.4Hz), 4.20 (2H, J=5.6Hz), 5.60 (2H, br s), 6.29 (1H, d, J=3.2Hz), 6.42 (1H, t, J=5.6Hz), 6.62 (1H, d, J=3.2Hz), 7.02 (1H, br s), 7.92 (3H, br s)

Anal Calcd. for $C_{15}H_{22}N_6O_2S \cdot C_2O_4H_2$:
C 46.35; H 5.49; N 19.08
Found : C 46.12; H 5.88; N 19.15

Example 5 (6)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(n-heptylamino)methyleneamino]thiazole

m.p.: 141-143°C

IR (Nujol) : 3250, 1670 cm^{-1}

NMR (DMSO-d_6, δ) : 0.86 (3H, t, J=6.7Hz), 1.28 (8H, br s), 1.40-1.60 (2H, m), 3.10-3.20 (2H, m), 4.19 (2H, d, J=5.5Hz), 5.57 (2H, s), 6.25 (1H, d, J=3.2Hz), 6.39 (1H, t, J=5.5Hz), 6.53 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.31 (3H, br s)

Anal Calcd. for $C_{17}H_{26}N_6O_2S$:
C 53.94; H 6.92; N 22.20
Found : C 54.18; H 7.22; N 21.92

Example 5 (7)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(n-octylamino)methyleneamino]thiazole

m.p.: 124-126°C

IR (Nujol) : 3300, 1640 cm^{-1}

NMR (DMSO-d_6, δ) : 0.85 (3H, t, J=6.7Hz), 1.20-1.38 (10H, m), 1.40-1.60 (2H, m), 3.15 (2H, q, J=5.6Hz), 4.19 (2H, d, J=5.5Hz), 5.57 (2H, s), 6.25 (1H, d, J=3.2Hz), 6.38 (1H, t, J=5.5Hz), 6.53 (1H, d, J=3.2Hz), 6.76 (1H, s), 7.31 (3H,

br s)

Anal Calcd. for $C_{18}H_{28}N_6O_2S \cdot 1/4H_2O$:
C 54.45; H 7.24; N 21.17
Found : C 54.45; H 7.37; N 21.04

Example 5 (8)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino){2-(2-methylthiazol-5-yl)ethylamino}methyleneamino]thiazole

m.p. : 177-179°C

IR (Nujol) : 3350, 1650, 1600, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 2.58 (3H, s), 3.02 (2H, t, J=6.5Hz), 3.30-3.50 (2H, m), 4.20 (2H, d, J=5.4Hz), 5.59 (2H, s), 6.27 (1H, d, J=3.2Hz), 6.43 (1H, t, J=5.4Hz), 6.59 (1H, d, J=3.2Hz), 6.88 (1H, s), 7.42 (1H, s), 7.69 (3H, br s)

Example 5 (9)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-n-propoxybenzylamino)methyleneamino]thiazole

m.p. : 147-148°C

IR (Nujol) : 3350, 1650, 1600, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 0.99 (3H, t, J=7.3Hz), 1.71-1.81 (2H, m), 3.97 (2H, t, J=6.4Hz), 4.18 (2H, d, J=5.7Hz), 4.39 (2H, d, J=5.6Hz), 5.56 (2H, s), 6.23 (1H, d, J=3.2Hz), 6.37 (1H, t, J=5.7Hz), 6.49 (1H, d, J=3.2Hz), 6.77 (1H, s), 6.88-7.01 (2H, m), 7.21-7.28 (2H, m), 7.45 (3H, br s)

Example 5 (10)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(3-phenylpropylamino)methyleneamino]thiazole

m.p. : 197-198°C

NMR (DMSO-d_6, δ) : 1.82-1.98 (2H, m), 2.70 (2H, t, J=7.2Hz), 3.25-3.35 (2H, m), 4.21 (2H, d, J=5.6Hz), 5.61 (2H, br s), 6.31 (1H, d,

J=3.2Hz), 6.46 (1H, t, J=5.6Hz), 6.82 (1H, d, J=3.2Hz), 7.18-7.33 (6H, m), 8.54 (3H, br s)

Example 5 (11)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-phenethylamino)methyleneamino]thiazole

m.p. : 137-138°C

IR (Nujol) : 3400, 1700, 1640, 1600, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 2.84 (2H, t, J=7.3Hz), 3.40-3.58 (2H, m), 4.19 (2H, d, J=5.7Hz), 5.57 (2H, s), 6.26 (1H, t, J=3.2Hz), 6.39 (1H, t, J=5.7Hz), 6.52 (1H, d, J=3.2Hz), 6.86 (1H, s), 7.20-7.38 (5H, m), 7.59 (3H, br s)

Anal Calcd. for $C_{18}H_{20}N_6O_2S \cdot 3/2H_2O$:
C 52.54; H 5.63; N 20.42
Found : C 52.46; H 5.24; N 20.86

Example 5 (12)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(4-methylpentylamino)methyleneamino]thiazole

m.p. : 123-124°C

IR (Nujol) : 3200, 1630, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (6H, d, J=6.7Hz), 1.18-1.29 (2H, m), 1.25-1.62 (3H, m), 3.18-3.40 (2H, m), 4.20 (2H, d, J=5.7Hz), 5.60 (2H, br s), 6.29 (1H, d, J=3.2Hz), 6.44 (1H, t, J=5.7Hz), 6.70 (1H, d, J=3.2Hz), 7.07 (1H, s), 8.02 (3H, br s)

Example 5 (13)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(cyclopropylmethylamino)methyleneamino]thiazole

m.p. : 166-167°C

IR (Nujol) : 3250, 1630, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 0.01-0.05 (2H, m), 0.23-0.31 (2H, m), 0.75-0.92 (1H, m), 2.82-2.88 (2H, m),

3.98 (2H, d, J=5.6Hz), 5.37 (2H, s), 6.05 (1H, d, J=3.2Hz), 6.19 (1H, t, J=5.6Hz), 6.36 (1H, d, J=3.2Hz), 6.57 (1H, s), 7.14 (3H, br s)

Example 5 (14)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(3,3-dimethylbutylamino)methyleneamino]thiazole

m.p. : 193-194°C

IR (Nujol) : 3300, 3100, 1690, 1640, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 0.95 (9H, s), 1.54 (2H, t, J=8.0Hz), 3.27-3.38 (2H, m), 4.21 (2H, d, J=5.6Hz), 5.61 (2H, s), 6.32 (1H, d, J=3.2Hz), 6.47 (1H, t, J=5.6Hz), 6.79 (1H, d, J=3.2Hz), 7.26 (1H, s), 8.44 (3H, br s)

Anal Calcd. for $C_{16}H_{24}N_6O_2S$: C 52.73; H 6.64; N 23.06

Found : C 52.22; H 6.87; N 23.20

Example 5 (15)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-cyclohexylethylamino)methyleneamino]thiazole

m.p. : 187-188°C

IR (Nujol) : 3400, 1700, 1635, 1610, 1525 cm^{-1}

NMR (DMSO-d_6, δ) : 0.83-1.05 (2H, m), 1.07-1.25 (4H, m), 1.27-1.76 (7H, m), 3.28-3.46 (2H, m), 4.21 (2H, d, J=5.5Hz), 5.63 (2H, br s), 6.32 (1H, d, J=3.3Hz), 6.48 (1H, t, J=5.5Hz), 6.80 (1H, d, J=3.3Hz), 7.30 (1H, s), 8.51 (3H, br s)

Anal Calcd. for $C_{18}H_{26}N_6O_2S$: C 55.36; H 6.71; N 21.52

Found : C 55.29; H 6.40; N 21.68

Example 5 (16)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-methoxyphenethylamino)methyleneamino]thiazole

m.p. : 165-169°C

IR (Nujol) : 3450, 1650, 1590, 1550 cm^{-1}

NMR (DMSO-d_6, δ) : 2.81 (2H, t, J=7.2Hz), 3.36-3.42 (2H, m), 3.79 (3H, s), 4.19 (2H, d, J=5.5Hz), 5.59 (2H, s), 6.26 (1H, d, J=3.2Hz), 6.41 (1H, t, J=5.5Hz), 6.51 (1H, d, J=3.2Hz), 6.80 (1H, s), 6.84-6.99 (2H, m), 7.18-7.25 (2H, m), 7.46 (3H, br s)

Anal Calcd. for $C_{19}H_{22}N_6O_3S \cdot 4/5H_2O$:
C 53.21; H 5.55; N 19.59
Found : C 53.16; H 5.51; N 19.68

Example 5 (17)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-methylphenethylamino)methyleneamino]thiazole

m.p. : 169-172°C

IR (Nujol) : 3350, 1630, 1600, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 2.33 (3H, s), 2.83 (2H, t, J=6.9Hz), 3.29-3.43 (2H, m), 4.20 (2H, d, J=5.7Hz), 5.60 (2H, s), 6.26 (1H, d, J=3.2Hz), 6.44 (1H, t, J=5.7Hz), 6.56 (1H, d, J=3.2Hz), 6.89 (1H, s), 7.09-7.23 (4H, m), 7.70 (3H, br s)

Anal Calcd. for $C_{19}H_{22}N_6O_2S$:
C 57.27; H 5.56; N 21.09
Found : C 56.97; H 5.35; N 21.08

Example 5 (18)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(2-phenylbenzylamino)methyleneamino]thiazole

m.p. : 137-138°C

IR (Nujol) : 3350, 1630, 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 4.18 (2H, d, J=5.6Hz), 4.32 (2H, d, J=5.3Hz), 5.61 (2H, br s), 6.23 (1H, d, J=3.2Hz), 6.44 (1H, t, J=5.6Hz), 6.42-6.52 (1H,

m), 6.78 (1H, s), 7.22-7.26 (1H, m), 7.33-7.52 (11H, m)

Anal Calcd. for $C_{23}H_{22}N_6O_2S$:
C 61.87; H 4.97; N 18.82
Found : C 61.79; H 4.44; N 18.62

Example 5 (19)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(8-quinolylmethylamino)methyleneamino]thiazole

m.p. : 187-188°C

IR (Nujol) : 3300, 1660, 1590, 1515 cm^{-1}

NMR (DMSO-d_6, δ) : 4.18 (2H, d, J=5.6Hz), 5.03 (2H, d, J=5.8Hz), 5.59 (2H, br s), 6.24 (1H, d, J=3.0Hz), 6.40 (1H, t, J=5.8Hz), 6.45 (1H, d, J=3.0Hz), 6.79 (1H, s), 7.45-7.68 (5H, m), 7.77 (1H, d, J=7.0Hz), 7.94 (1H, d, J=8.1Hz), 8.43 (1H, d, J=6.8Hz), 8.98-9.00 (1H, m)

Anal Calcd. for $C_{20}H_{19}N_7O_2S \cdot H_2O$:
C 54.66; H 4.82; N 22.75
Found : C 54.99; N 4.55; N 22.43

Example 5 (20)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(1-naphthalenylmethylamino)methyleneamino]thiazole

m.p. : 189-192°C

IR (Nujol) : 3300, 1650, 1590, 1520 cm^{-1}

NMR (DMSO-d_6, δ) : 4.17 (2H, d, J=5.7Hz), 5.03 (2H, d, J=5.7Hz), 5.58 (2H, br s), 6.20 (1H, d, J=3.2Hz), 6.32 (1H, d, J=3.2Hz), 6.42 (1H, t, J=5.7Hz), 7.04 (1H, s), 7.48-7.65 (4H, m), 7.91-8.03 (2H, m), 8.12-8.17 (4H, m)

Anal Calcd. for $C_{21}H_{20}N_6O_2S \cdot 2.5H_2O$:
C 54.18; H 5.41; N 18.05
Found : C 54.15; H 5.64; N 18.02

Example 5 (21)

4-(5-Ureidomethylfuran-2-yl)-2-[(amino)(n-pentylamino)methyleneamino]thiazole

m.p. : 185-188°C

IR (Nujol) : 3270, 1680, 1630, 1555 cm^{-1}

NMR (DMSO-d_6, δ) : 0.88 (3H, t, J=7.0Hz), 1.18-1.43 (4H, m), 1.45-1.68 (2H, m), 3.18-3.36 (2H, m), 4.21 (2H, d, J=5.7Hz), 5.63 (2H, br s), 6.29 (1H, d, J=3.2Hz), 6.48 (1H, t, J=5.7Hz), 6.67 (1H, d, J=3.2Hz), 7.02 (1H, s), 7.94 (1H, br s)

MASS (m/z) : 351 (M^++1)

Example 6 (1)

A mixture of N-[(amino)(2-chlorobenzylamino)-methylene]thiourea (728 mg), 2-acetylaminomethyl-5-(chloroacetyl)furan (646 mg), sodium hydrogen carbonate (756 mg) in methanol (15 ml) was refluxed for 1 hour. The reaction mixture was evaporated in vacuo. The residue was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over anhydrous magnesium sulfate and treated with activated charcoal. After filtered off, the filtrate was evaporated in vacuo. The residue was purified by chromatography on silica gel eluting with (20% ethyl acetate/chloroform) to give 4-(5-acetylaminomethylfuran-2-yl)-2-[(amino)(2-chlorobenzylamino)methyleneamino]-thiazole (635 mg).

m.p.: 164-165°C

IR (Nujol) : 3300, 1670, 1640, 1595 cm^{-1}

NMR (DMSO-d_6, δ) : 1.85 (3H, s), 4.26 (2H, d, J=5.5Hz), 4.49 (2H, d, J=5.8Hz), 6.28 (1H, d, J=3.2Hz), 6.56 (1H, d, J=3.0Hz), 6.81 (1H, s), 7.27-7.49 (5H, m), 7.57 (1H, br s), 8.34 (1H, d, J=5.8Hz)

The following compounds were obtained according to a similar manner to that of Example 6 (1).

Example 6 (2)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(2-methoxyphenylethylamino)methyleneamino]thiazole oxalate

m.p.: 188-190°C

IR (Nujol) : 3430, 3300, 1735, 1700, 1645, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 2.88 (2H, t, J=6.8Hz), 3.49-3.51 (2H, m), 3.77 (3H, s), 4.28 (2H, d, J=5.5Hz), 6.33 (1H, d, J=3.2Hz), 6.51 (1H, d, J=3.2Hz), 6.83-7.22 (4H, m), 7.25 (1H, s), 8.37 (1H, t, J=5.5Hz)

Example 6 (3)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-ethoxyanilino)methyleneamino]thiazole

m.p. : 108-110°C

IR (Nujol) : 3150, 1620, 1560, 1490 cm^{-1}

NMR (DMSO-d_6, δ) : 1.30 (3H, t, J=6.9Hz), 1.85 (3H, s), 3.98 (2H, q, J=6.9Hz), 4.26 (2H, d, J=5.5Hz), 6.30 (1H, d, J=3.1Hz), 6.61 (1H, d, J=3.1Hz), 6.87 (2H, d, J=8.9Hz), 6.89 (1H, s), 7.32 (2H, d, J=8.9Hz), 7.63 (2H, br s), 8.34 (1H, t, J=5.5Hz), 8.75 (1H, br s)

Example 6 (4)

4-(5-Acetylaminomethylfuran-2-yl)-2-[(amino)(4-chloroanilino)methyleneamino]thiazole

m.p. : 191-192°C

IR (Nujol) : 3350, 1620, 1510 cm^{-1}

NMR (DMSO-d_6, δ) : 1.86 (3H, s), 4.28 (2H, d, J=5.5Hz), 6.32 (1H, d, J=3.2Hz), 6.68 (1H, d, J=3.2Hz), 6.98 (1H, s), 7.35 (2H, d, J=8.8Hz),

7.54 (2H, d, J=8.8Hz), 7.81 (2H, br s), 8.36 (1H, t, J=5.5Hz), 8.95 (1H, s)

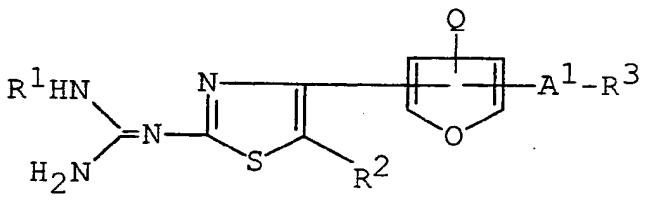
Anal Calcd. for $C_{17}H_{16}ClN_5O_2S$:

C 52.37; H 4.14; N 17.96

Found : C 51.93; H 3.96; N 17.76

C L A I M S

1. A furylthiazole derivative of the following formula :



wherein

R^1 is n-pentyl, branched(lower)alkyl,
branched(lower)alkenyl, lower alkenyl having
(lower)alkoxy, higher alkyl,
cyclo(lower)alkyl(lower)alkyl,
cyclo(lower)alkylidene(lower)alkyl,
cyclo(lower)alkenyl(lower)alkyl,
lower alkylthio(lower)alkyl,
aryl which may have one or more suitable
substituent(s),
ar(lower)alkyl which may have one or more
suitable substituent(s),
aryloxy(lower)alkyl which may have one
or more suitable substituent(s),
ar(lower)alkoxy(lower)alkyl which may have one or
more suitable substituent(s),
higher alkenyl which may have one or more suitable
substituent(s),
propoxypropyl, ethoxypropyl, butoxypropyl,
propoxyethyl, butoxyethyl, butoxybutyl,
methoxybutyl, ethoxybutyl,
lower alkoxy(lower)alkoxy(lower)alkyl,
arylamino(lower)alkyl which may have one or
more suitable substituent(s),
pyridin-4-yl(lower)alkyl,
pyridin-3-yl(lower)alkyl,

lower alkyl-substituted pyridyl(lower)alkyl,
imidazolyl(lower)alkyl or
a group of the formula :

$$-A^2-R^4$$

[wherein
A^2 is lower alkylene or lower alkenylene, and
R^4 is unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s),
unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) which may have one or more suitable substituent(s),
unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atom(s),
saturated 3 to 8-membered heteromonocyclic group containing 1 to 2 oxygen atom(s),
saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s)
or
unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) which may have one or more suitable substituent(s),]

R^2 is hydrogen or lower alkyl,
R^3 is amino or acylamino,
A^1 is lower alkyl, and
Q is hydrogen or lower alkyl,
and a pharmaceutically acceptable salt thereof.

2. A compound of claim 1, wherein
R^1 is n-pentyl, branched(lower)alkyl, branched(lower)-alkenyl, lower alkenyl having (lower)alkoxy,

higher alkyl, propoxypropyl, ethoxypropyl, butoxypropyl, propoxyethyl, butoxyethyl, butoxybutyl, methoxybutyl, ethoxybutyl, pyridin-4-yl(lower)-alkyl, pyridin-3-yl(lower)alkyl, lower alkyl-substituted pyridyl(lower)alkyl, imidazolyl(lower)alkyl, or a group of the formula :

$$-A^2-R^4$$

[wherein
A^2 is lower alkylene or lower alkenylene, and
R^4 is furanyl, thienyl, indolyl, tetrahydropyranylidene, methylthiazolyl, piperidyl, or quinolyl,]

R^2 is hydrogen or lower alkyl,
R^3 is amino or acylamino,
A^1 is lower alkyl, and
Q is hydrogen or lower alkyl.

3. A compound of claim 2, wherein
R^1 is n-pentyl, branched(lower)alkyl, branched(lower)alkenyl, lower alkenyl-having(lower)alkoxy, higher alkyl, propoxypropyl, ethoxypropyl, butoxypropyl, propoxyethyl, butoxyethyl, butoxybutyl, methoxybutyl, ethoxybutyl, or a group of the formula :

$$-A^2-R^4$$

[wherein A^2 is lower alkylene, and
R^4 is furanyl, thienyl or quinolyl,]

R^2 is hydrogen,
R^3 is ureido or lower alkanoylamino and

Q is hydrogen.

4. A compound of claim 1, wherein
R^1 is cyclo(lower)alkyl(lower)alkyl,
cyclo(lower)alkylidene(lower)alkyl,
cyclo(lower)alkenyl(lower)alkyl,
lower alkylthio(lower)alkyl,
aryl which may have one or more suitable substituent(s),
ar(lower)alkyl which may have one or more suitable substituent(s),
aryloxy(lower)alkyl which may have one or more suitable substituent(s),
ar(lower)alkoxy(lower)alkyl which may have one or more suitable substituent(s),
higher alkenyl which may have one or more suitable substituent(s),
lower alkoxy(lower)alkoxy(lower)alkyl, and
arylamino(lower)alkyl which may have one or more suitable substituent(s),
R^2 is hydrogen or lower alkyl,
R^3 is amino or acylamino,
A^1 is lower alkyl, and
Q is hydrogen or lower alkyl.

5. A compound of claim 4, wherein
R^1 is cyclo(lower)alkyl(lower)alkyl;
cyclo(lower)alkylidene(lower)alkyl;
cyclo(lower)alkenyl(lower)alkyl;
phenyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono or di-

(lower)alkylaminosulfonyl, lower alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono or di-(lower)alkylcarbamoyl(lower)alkoxy;

phenyl(lower)alkyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy;

phenoxy(lower)alkyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower-alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy; and

phenyl(lower)alkoxy(lower)alkyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower-alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy;

R^2 is hydrogen,

R^3 is acylamino, and

Q is hydrogen.

6. A compound of claim 5, wherein

R^1 is phenyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic (lower)alkyl, mono or di-(lower)alkylaminosulfonyl, lower-alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono or di-(lower)alkylcarbamoyl(lower)alkoxy;

phenyl(lower)alkyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy;

phenoxy(lower)alkyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower-alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy; and

phenyl(lower)alkoxy(lower)alkyl which may have 1 to

3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower-alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy; and

R^3 is ureido or lower alkanoylamino.

7. A compound of claim 6, wherein

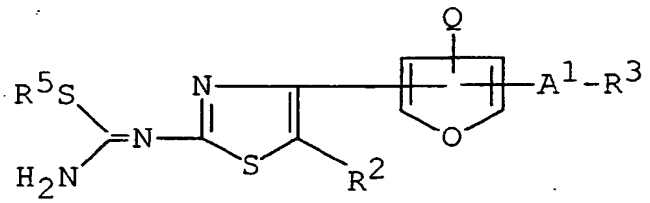
R^1 is phenyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower) alkylaminosulfonyl, lower alkoxy(lower)alkoxy, protected carboxy(lower)alkoxy, and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy;

phenyl(lower)alkyl which may have 1 to 3 suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, nitro, halogen, and sulfamoyl, aryloxy(lower)alkyl, heterocyclic group, heterocyclic(lower)alkyl, mono- or di-(lower)alkylaminosulfonyl, lower-alkoxy(lower)alkoxy, protected-carboxy(lower)alkoxy and mono- or di-(lower)alkylcarbamoyl(lower)alkoxy.

8. A process for preparing a compound of claim 1 or a salt thereof,

which comprises,

(1) reacting a compound of the formula :



wherein R^2, R^3, A^1 and Q are each as defined above,

and

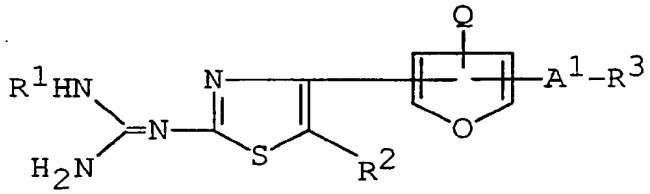
R^5 is lower alkyl,

or a salt thereof, with a compound of the formula :

$$R^1\text{-}NH_2$$

wherein R^1 is as defined above,

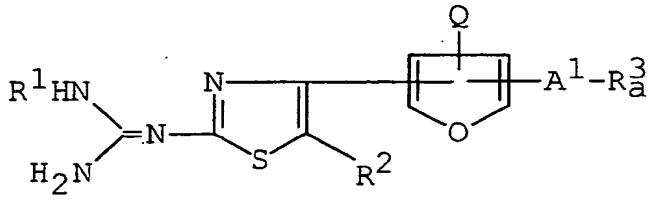
or a salt thereof, to give a compound of the formula :



wherein R^1, R^2, R^3, A^1 and Q are each as defined above,

or a salt thereof, or

(2) subjecting a compound of the formula :

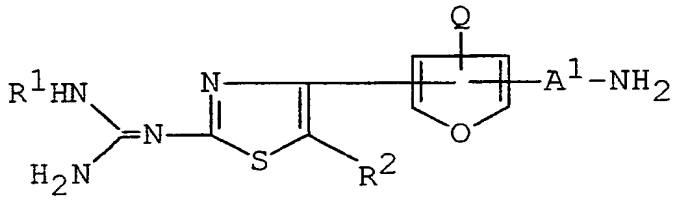


wherein R^1, R^2, A^1 and Q are each as defined above,

and

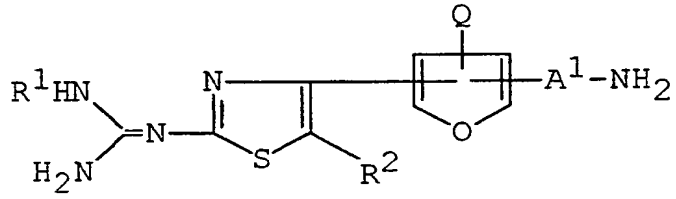
R_a^3 is acylamino,

or a salt thereof, to deacylation reaction, to give a compound of the formula :

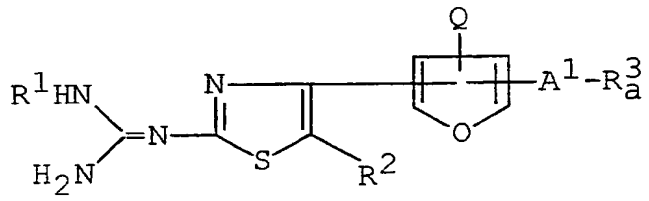


wherein R^1, R^2, A^1 and Q are each as defined above, or a salt thereof, or

(3) reacting a compound of the formula :

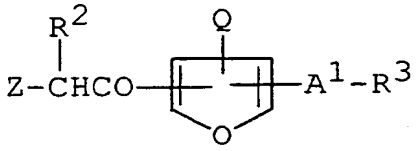


wherein R^1, R^2, A^1 and Q are each as defined above, or a salt thereof, to acylation reaction, to give a compound of the formula :

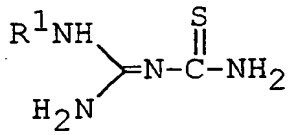


wherein R^1, R^2, R_a^3, A^1 and Q are each as defined above, or a salt thereof, or

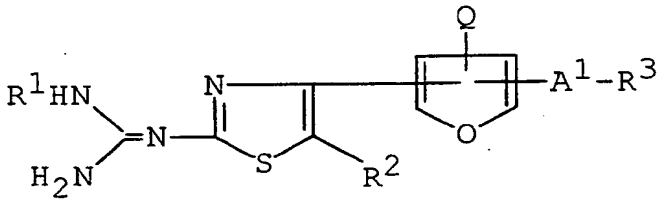
(4) reacting a compound of the formula :



wherein R^2, R^3, A^1 and Q are each as defined above,
and
Z is acid residue,
or a salt thereof, with a compound of the formula :



wherein R^1 is as defined above, or a salt thereof,
to give a compound of the formula :



wherein R^1, R^2, R^3, A^1 and Q are each as defined above,
or a salt thereof.

9. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers.

10. A method for the prevention and/or the treatment of ulcer which comprises administering a compound of claim 1 or a pharmaceutically acceptable salt thereof to a human being or an animal.

11. A compound of claim 1 or a pharmaceutically acceptable salt thereof for use as antiulcer agent, H_2-receptor antagonist or antimicrobial agent.

12. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof for the manufacture of an antiulcer agent, H_2-receptor antagonist or antimicrobial agent.

INTERNATIONAL SEARCH REPORT

Inter. ional Application No
PCT/JP 94/02278

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D417/04 A61K31/425 C07D417/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 355 612 (FUJISAWA PHARMACEUTICAL CO.,LTD) 28 February 1990 see claims ---	1-12
X	WO,A,93 03028 (FUJISAWA PHARMACEUTICAL CO.,LTD) 18 February 1993 see claims ---	1-12
X	US,A,4 814 341 (LAWRENCE A. REITER) 21 March 1989 see claims ---	1-12
P,X	WO,A,94 03450 (FUJISAWA PHARMACEUTICAL CO.,LTD) 17 February 1994 see claims -----	1-12

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 1995	22. 02. 95
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Authorized officer Henry, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 94/ 02278

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Althogh claim 10 is directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compounds.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Inter. ...nal Application No
PCT/JP 94/02278

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-0355612	28-02-90	AT-T-	109144	15-08-94
		AU-A-	3934689	15-02-90
		DE-D-	68917049	01-09-94
		DE-T-	68917049	05-01-95
		JP-A-	2072177	12-03-90
		US-A-	5308857	03-05-94
WO-A-9303028	18-02-93	CA-A-	2114651	18-02-93
		EP-A-	0598906	01-06-94
		WO-A-	9403450	17-02-94
		JP-T-	6509353	20-10-94
US-A-4814341	21-03-89	NONE		
WO-A-9403450	17-02-94	CA-A-	2114651	18-02-93
		EP-A-	0598906	01-06-94
		WO-A-	9303028	18-02-93
		JP-T-	6509353	20-10-94